EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	741	(Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperdylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:23
S2	115	S1 AND ((salt or salts or "free base" or acetate) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperdylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:23

S3	54	S1 AND ((dimorph or dimorphs or dimorphic or dimorphism or dimorphous or trimorph or trimorphs or trimorphic or trimorphism or trimorphous or polymorph or polymorphs or polymorphic or polymorphism or polymorphous or pseudopolymorph or pseudopolymorphs or pseudopolymorphic or pseudopolymorphism or pseudopolymorphous or pleomorph or pleomorphs or pleomorphic or pleomorphism or pleomorphous or conformer or conformers or conformeric or conformerism or conformation or conformations or conformational or isomer or isomers isomeric or isomerism or isomorph or isomorphs or isomorphic or isomorphism or isomorphous or enantiomer or enantiomers enantiomeric or enantiomerism or enantiopure or enantiomorph or enantiomorphs or enantiomorphic or enantiomorphism or enantiomorphous or stereoisomer or stereoisomers stereoisomeric or stereoisomerism or stereoisomorph or stereoisomorphs or stereoisomorphic or stereoisomorphism or stereoisomorphous or diastereoisomer or diastereoisomers diastereoisomeric or diastereoisomerism or diastereomorph or diastereomorphs or diastereomorphic or diastereomorphism or diastereomorphous or diastereomer or diastereomers or diastereomeric or diastereomerism or tautomer or tautomers or tautomeric or tautomerism or tautomorph or tautomorphs or tautomorphic or tautomorphism or tautomorphous or stereochemistry or stereochemical) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:23

S4	9	S1 AND (("form I" or "form II" or "form III" or "form IV" or "form V" or "form VI" or "form 1" or "form 2" or "form 3" or "form 4" or "form 5" or "form 6") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:32

S5	13	S1 AND ((crystal or crystals or crystalline or crystallinity or crystallize or crystallizes or crystallized or crystallization or microcrystal or microcrystals or microcrystalline or microcrystallinity or microcrystallize or microcrystallizes or microcrystallized or microcrystallization or semicrystal or semicrystals or semicrystalline or semicrystallinity or semicrystallize or semicrystallizes or semicrystallized or semicrystallization or recrystallize or recrystallizes or recrystallized or recrystallization or crystallography or crystallographic or "x-ray diffraction") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:24

S6	202	S1 AND ((composition or formulation or preparation or mixture or admixture or immixture or preparation OR compound or material or substance or ingredient or drug or prodrug or "pro-drug" or medicament or medicine or medication or medicinal or pharmaceutic$ or pharmacologic$ or therapeutic$ or biologic or bioactive or "bio-active" or nutraceutic$ or "active agent" or "active ingredient" or "active principle" or "active substance" or "active compound" or "active material" or "bioactive agent" or "bioactive ingredient" or "bioactive principle" or "bioactive substance" or "bioactive compound" or "bioactive material" or "pharmaceutically active" or "beneficial agent" or "beneficial ingredient" or "beneficial principle" or "beneficial substance" or "beneficial compound") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:24

S7	106	S1 AND ((method or methods or procedure or process or processed or processes or processing or preparing or prepared or making or made or manufacturing or manufactured or synthesizing or synthesized or producing or produced or formulating or formulated or developing or developed or creating or created or mixing or mixed or admixing or admixed or blending or blended or combining or combined or dispersing or dispersed or adding or added or incorporating or incorporated or recovering or recovered or obtaining or obtained or isolating or isolated or separating or separated or filtering or filtered or purifying or purified or drying or dried or solvation or dissolve or dissolved or dissolves or dissolving or dissolvation or dissolution or dissolvative or resolve or resolved or resolves or resolving or resolvation or solubilize or solubilized or solubilizes or solubilizing or solubilization or antisolvation or "anti-solvation" or insolvation or "in-solvation" or nonsolvation or "non-solvation" or precipitate or precipitated or precipitates or precipitating or precipitation or crystallize or crystallizes or crystallized or crystallizing or crystallization or microcrystallize or microcrystallizes or microcrystallized or microcrystallizing or microcrystallization or semicrystallize or semicrystallizes or semicrystallized or semimicrocrystalizing or semicrystallization or recrystallize or recrystallizes or recrystallized or recrystallizing or recrystallization or braying or brayed or crushing or crushed or granulating or granulated or grinding or grinded or ground or milling or milled or powdering or powdered or pulverizing or pulverized or triturating or triturated or homogenizing or homogenized) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:27

S8	240	S2 OR S3 OR S4 OR S5 OR S6 OR S7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:55

EAST Search History

S9	62	S8 AND (("alkali metal" or "alkali element" or "alkali cation" or "monovalent cation" or "mono-valent cation" or lithium or sodium or potassium or rubidium or cesium or francium OR "alkaline earth metal" or "alkaline earth element" or "alkaline earth cation" or "divalent cation" or "di-valent cation" or beryllium or magnesium or calcium or strontium or barium or radium) NEAR10 (oxide or hydroxide or carbonate or bicarbonate or hydrogencarbonate) NEAR10 (base or basic or water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:28

S10	55	S8 AND ((strong or "sodium hydride" or "lithium diisopropylamide" or "sodium amide" or weak or alanine or ammonia or "magnesium hydroxide" or methylamine or pyridine) NEAR5 (base or basic or water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

S11	61	S8 AND ((base or basic) NEAR5 (water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

EAST Search History

S12	33	S8 AND ((hydrocarbon or hydrocarbons or alkane or alkanes or isoalkane or isoalkanes or "n-alkane" or "n-alkanes" or methane or ethane or propane or butane or "n-butane" or pentane or "n-pentane" or hexane or "n-hexane" or heptane or "n-heptane" or octane or "n-octane" or nonane or "n-nonane" or decane or "n-decane" or undecane or "n-undecane" or dodecane or "n-dodecane" or gasoline or petroleum or turpentine) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

S13	29	S8 AND ((aromatic or benzene or benzol or benzine or toluene or toluol or methylbenzene or xylene or xylol or dimethylbenzene) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

S14	110	S8 AND ((alcohol or alcoholic or ethanol or "ethyl alcohol" or methanol or "methyl alcohol" or propanol or "propyl alcohol" or isopropanol or "isopropyl alcohol" or "iso-propanol" or "iso-propyl alcohol" or "2-propanol" or "2-propyl alcohol" or butanol or "butyl alcohol" or isobutanol or "isobutyl alcohol" or "iso-butanol" or "iso-butyl alcohol" or "polyhydric alcohol") NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

S15	50	S8 AND ((ester or "methyl acetate" or "acetic acid methyl ester" or "methyl ethanoate" or "methyl acetoacetate" or "ethyl acetate" or "acetic acid ethyl ester" or "ethyl ethanoate" or "acetic ether" or "acetic ester" or "ethyl acetoacetate" or "propyl acetate" or "propyl ethanoate" or "isopropyl acetate" or "iso-propyl acetate" or "isopropyl ethanoate" or "iso-propyl ethanoate" or "butyl acetate" or "butyl ethanoate" or "isobutyl acetate" or "iso-butyl acetate" or "isobutyl ethanoate" or "iso-butyl ethanoate" or "methylpropyl ethanoate" or "pentyl acetate" or "pentyl ethanoate" or "isopentyl acetate" or "iso-pentyl acetate" or "isopentyl ethanoate" or "iso-pentyl ethanoate" or "amyl acetate") NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:29

S16	52	S8 AND (("CH3Cl" or "CH3F" or "CH3Br" or "CH3I" or monochloromethane or chloromethane or "methyl chloride" or monofluoromethane or fluoromethane or "methyl fluoride" or monobromomethane or bromomethane or "methyl bromide" or monoiodomethane or iodomethane or "methyl iodide" OR "CH2Cl2" or "CH2F2" or "CH2Br2" or "CH2I2" or dichloromethane or "methylene chloride" or difluoromethane or "methylene fluoride" or dibromomethane or "methylene bromide" or diiodomethane or "methylene iodide" OR "CHCl3" or "CHF3" or "CHBr3" or "CHI3" or trichloromethane or chloroform or trifluoromethane or tribromomethane or triiodomethane OR "CCl4" or "CF4" or "CBr4" or "CI4" or "carbon tetrafluoride" or tetrafluoromethane or "carbon tetrachloride" or tetrachloromethane or "carbon tetrabromide" or tetrabromomethane or "carbon tetraiodide" or tetraiodomethane) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:30

S17	132	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:53
S18	8	S4 AND S17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:35
S19	9	S4 OR S18	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/08 21:35
S20	741	(Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:55

S21	115	S20 AND ((salt or salts or "free base" or acetate) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperdylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

EAST Search History

S22	54	S20 AND ((dimorph or dimorphs or dimorphic or dimorphism or dimorphous or trimorph or trimorphs or trimorphic or trimorphism or trimorphous or polymorph or polymorphs or polymorphic or polymorphism or polymorphous or pseudopolymorph or pseudopolymorphs or pseudopolymorphic or pseudopolymorphism or pseudopolymorphous or pleomorph or pleomorphs or pleomorphic or pleomorphism or pleomorphous or conformer or conformers or conformeric or conformerism or conformation or conformations or conformational or isomer or isomers isomeric or isomerism or isomorph or isomorphs or isomorphic or isomorphism or isomorphous or enantiomer or enantiomers enantiomeric or enantiomerism or enantiopure or enantiomorph or enantiomorphs or enantiomorphic or enantiomorphism or enantiomorphous or stereoisomer or stereoisomers stereoisomeric or stereoisomerism or stereoisomorph or stereoisomorphs or stereoisomorphic or stereoisomorphism or stereoisomorphous or diastereoisomer or diastereoisomers diastereoisomeric or diastereoisomerism or diastereomorph or diastereomorphs or diastereomorphic or diastereomorphism or diastereomorphous or diastereomer or diastereomers or diastereomeric or diastereomerism or tautomer or tautomers or tautomeric or tautomerism or tautomorph or tautomorphs or tautomorphic or tautomorphism or tautomorphous or stereochemistry or stereochemical) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidyli dene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylid ene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S23	9	S20 AND (("form I" or "form II" or "form III" or "form IV" or "form V" or "form VI" or "form 1" or "form 2" or "form 3" or "form 4" or "form 5" or "form 6") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperdyli dene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylid ene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S24	13	S20 AND ((crystal or crystals or crystalline or crystallinity or crystallize or crystallizes or crystallized or crystallization or microcrystal or microcrystals or microcrystalline or microcrystallinity or microcrystallize or microcrystallizes or microcrystallized or microcrystallization or semicrystal or semicrystals or semicrystalline or semicrystallinity or semicrystallize or semicrystallizes or semicrystallized or semicrystallization or recrystallize or recrystallizes or recrystallized or recrystallization or crystallography or crystallographic or "x-ray diffraction") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperdylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperdylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S25	202	S20 AND ((composition or formulation or preparation or mixture or admixture or immixture or preparation OR compound or material or substance or ingredient or drug or prodrug or "pro-drug" or medicament or medicine or medication or medicinal or pharmaceutic$ or pharmacologic$ or therapeutic$ or biologic or bioactive or "bio-active" or nutraceutic$ or "active agent" or "active ingredient" or "active principle" or "active substance" or "active compound" or "active material" or "bioactive agent" or "bioactive ingredient" or "bioactive principle" or "bioactive substance" or "bioactive compound" or "bioactive material" or "pharmaceutically active" or "beneficial agent" or "beneficial ingredient" or "beneficial principle" or "beneficial substance" or "beneficial compound") NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S26	106	S20 AND ((method or methods or procedure or process or processed or processes or processing or preparing or prepared or making or made or manufacturing or manufactured or synthesizing or synthesized or producing or produced or formulating or formulated or developing or developed or creating or created or mixing or mixed or admixing or admixed or blending or blended or combining or combined or dispersing or dispersed or adding or added or incorporating or incorporated or recovering or recovered or obtaining or obtained or isolating or isolated or separating or separated or filtering or filtered or purifying or purified or drying or dried or solvation or dissolve or dissolved or dissolves or dissolving or dissolvation or dissolution or dissolvative or resolve or resolved or resolves or resolving or resolution or solubilize or solubilized or solubilizes or solubilizing or solubilization or antisolvation or "anti-solvation" or insolvation or "in-solvation" or nonsolvation or "non-solvation" or precipitate or precipitated or precipitates or precipitating or precipitation or crystallize or crystallizes or crystallized or crystallizing or crystallization or microcrystallize or microcrystallizes or microcrystallized or microcrystalizing or microcrystallization or semicrystallize or semicrystallizes or semicrystallized or semimicrocrystalizing or semicrystallization or recrystallize or recrystallizes or recrystallized or recrystallizing or recrystallization or braying or brayed or crushing or crushed or granulating or granulated or grinding or grinded or ground or milling or milled or powdering or powdered or pulverizing or pulverized or triturating or triturated or homogenizing or homogenized) NEAR10 (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperidylidene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylidene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine"))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S27	240	S21 OR S22 OR S23 OR S24 OR S25 OR S26	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

EAST Search History

S28	62	S27 AND (("alkali metal" or "alkali element" or "alkali cation" or "monovalent cation" or "mono-valent cation" or lithium or sodium or potassium or rubidium or cesium or francium OR "alkaline earth metal" or "alkaline earth element" or "alkaline earth cation" or "divalent cation" or "di-valent cation" or beryllium or magnesium or calcium or strontium or barium or radium) NEAR10 (oxide or hydroxide or carbonate or bicarbonate or hydrogencarbonate) NEAR10 (base or basic or water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S29	55	S27 AND ((strong or "sodium hydride" or "lithium diisopropylamide" or "sodium amide" or weak or alanine or ammonia or "magnesium hydroxide" or methylamine or pyridine) NEAR5 (base or basic or water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S30	61	S27 AND ((base or basic) NEAR5 (water or aqueous or solution or "polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S31	33	S27 AND ((hydrocarbon or hydrocarbons or alkane or alkanes or isoalkane or isoalkanes or "n-alkane" or "n-alkanes" or methane or ethane or propane or butane or "n-butane" or pentane or "n-pentane" or hexane or "n-hexane" or heptane or "n-heptane" or octane or "n-octane" or nonane or "n-nonane" or decane or "n-decane" or undecane or "n-undecane" or dodecane or "n-dodecane" or gasoline or petroleum or turpentine) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S32	29	S27 AND ((aromatic or benzene or benzol or benzine or toluene or toluol or methylbenzene or xylene or xylol or dimethylbenzene) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S33	110	S27 AND ((alcohol or alcoholic or ethanol or "ethyl alcohol" or methanol or "methyl alcohol" or propanol or "propyl alcohol" or isopropanol or "isopropyl alcohol" or "iso-propanol" or "iso-propyl alcohol" or "2-propanol" or "2-propyl alcohol" or butanol or "butyl alcohol" or isobutanol or "isobutyl alcohol" or "iso-butanol" or "iso-butyl alcohol" or "polyhydric alcohol") NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S34	50	S27 AND ((ester or "methyl acetate" or "acetic acid methyl ester" or "methyl ethanoate" or "methyl acetoacetate" or "ethyl acetate" or "acetic acid ethyl ester" or "ethyl ethanoate" or "acetic ether" or "acetic ester" or "ethyl acetoacetate" or "propyl acetate" or "propyl ethanoate" or "isopropyl acetate" or "iso-propyl acetate" or "isopropyl ethanoate" or "iso-propyl ethanoate" or "butyl ethanoate" or "butyl acetate" or "butyl ethanoate" or "isobutyl acetate" or "iso-butyl acetate" or "isobutyl ethanoate" or "iso-butyl ethanoate" or "methylpropyl ethanoate" or "pentyl acetate" or "pentyl ethanoate" or "isopentyl acetate" or "iso-pentyl acetate" or "isopentyl ethanoate" or "iso-pentyl ethanoate" or "amyl acetate") NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated or precipitates or precipitating or precipitation))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

EAST Search History

S35	52	S27 AND (("CH3Cl" or "CH3F" or "CH3Br" or "CH3I" or monochloromethane or chloromethane or "methyl chloride" or monofluoromethane or fluoromethane or "methyl fluoride" or monobromomethane or bromomethane or "methyl bromide" or monoiodomethane or iodomethane or "methyl iodide" OR "CH2Cl2" or "CH2F2" or "CH2Br2" or "CH2I2" or dichloromethane or "methylene chloride" or difluoromethane or "methylene fluoride" or dibromomethane or "methylene bromide" or diiodomethane or "methylene iodide" OR "CHCl3" or "CHF3" or "CHBr3" or "CHI3" or trichloromethane or chloroform or trifluoromethane or tribromomethane or triiodomethane OR "CCl4" or "CF4" or "CBr4" or "CI4" or "carbon tetrafluoride" or tetrafluoromethane or "carbon tetrachloride" or tetrachloromethane or "carbon tetrabromide" or tetrabromomethane or "carbon tetraiodide" or tetraiodomethane) NEAR5 ("polar solvent" or "polar solvents" or "hydrophilic solvent" or "hydrophilic solvents" or "protic solvent" or "protic solvents" or "nonpolar solvent" or "non-polar solvent" or "nonpolar solvents" or "non-polar solvents" or "hydrophobic solvent" or "hydrophobic solvents" or "lipophilic solvent" or " lipophilic solvents" or "aprotic solvent" or "aprotic solvents" or solvent or solvation or solvency or dissolve or dissolved or dissolves or dissolving or dissolvable or dissolvability or dissolvent or dissolvation or dissolver or dissolution or dissolvative or diluent or dilutant or resolve or resolved or resolves or resolving or resolvable or resolvability or resolvation or resolvent or resolver or resoluble or resolubility or recrystallize or recrystallizes or recrystallized or recrystallization or solution or soluble or solubility or solubleness or solubly or solvable or solvability or solubilize or solubilized or solubilizes or solubilizing or solubilization or solubilizer or antisolvent or "anti-solvent" or antisolvation or "anti-solvation" or antisolvency or "anti-solvency" or insolvent or "in-solvent" or insolvation or "in-solvation" or insolvency or "in-solvency" or insoluble or insolubility or insolubleness or insolubly or nonsolvent or "non-solvent" or nonsolvation or "non-solvation" or nonsolvency or "non-solvency" or precipitate or precipitated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 11:29

S36	132	S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 12:43
S37	152	(S27 OR S36) AND @AY<="2003"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:55
S38	107	(S27 OR S36) AND @AD<="20030312"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 12:44
S39	13175	Schering.AS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:54
S40	93	S20 AND S39	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:54

S41	31	S40 AND (Desloratadine or Clarinex or Aerius or Azomyr or Descarboethoxyloratadine or Neoclarityn or Opulis or "8-chloro-6, 11-dihydro-11-(4-piperdyli dene)-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine" or "8-chloro-11-(4-piperidylid ene)-6, 11-dihydro-5H-benzo[5, 6]cyclohepta[1, 2-b]pyridine").CLM.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 16:02
S42	25	S41 AND @AY<="2003"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:56

S43	13	S42 AND (dimorph or dimorphs or dimorphic or dimorphism or dimorphous or trimorph or trimorphs or trimorphic or trimorphism or trimorphous or polymorph or polymorphs or polymorphic or polymorphism or polymorphous or pseudopolymorph or pseudopolymorphs or pseudopolymorphic or pseudopolymorphism or pseudopolymorphous or pleomorph or pleomorphs or pleomorphic or pleomorphism or pleomorphous or conformer or conformers or conformeric or conformerism or conformation or conformations or conformational or isomer or isomers isomeric or isomerism or isomorph or isomorphs or isomorphic or isomorphism or isomorphous or enantiomer or enantiomers enantiomeric or enantiomerism or enantiopure or enantiomorph or enantiomorphs or enantiomorphic or enantiomorphism or enantiomorphous or stereoisomer or stereoisomers stereoisomeric or stereoisomerism or stereoisomorph or stereoisomorphs or stereoisomorphic or stereoisomorphism or stereoisomorphous or diastereoisomer or diastereoisomers diastereoisomeric or diastereoisomerism or diastereomorph or diastereomorphs or diastereomorphic or diastereomorphism or diastereomorphous or diastereomer or diastereomers or diastereomeric or diastereomerism or tautomer or tautomers or tautomeric or tautomerism or tautomorph or tautomorphs or tautomorphic or tautomorphism or tautomorphous or stereochemistry or stereochemical)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/09 14:57

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=> S desloratadine/CN
L1           1 DESLORATADINE/CN

=> D L1

L1    ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN    100643-71-8  REGISTRY
ED    Entered STN:  01 Mar 1986
CN    5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-
      piperidinylidene)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN    8-Chloro-11-(4-piperidylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-
      b]pyridine
CN    Aerius
CN    Allex
CN    Azomyr
CN    Clarinex
CN    Descarboethoxyloratadine
CN    Desloratadine
CN    Neoclarityn
CN    NSC 675447
CN    Opulis
CN    Sch 34117
DR    381727-28-2
MF    C19 H19 Cl N2
CI    COM
SR    CA
LC    STN Files:   ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS,
        BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CIN,
        CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA,
        MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH,
        SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
          (*File contains numerically searchable property data)
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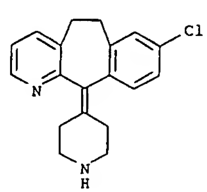

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

            398 REFERENCES IN FILE CA (1907 TO DATE)
              6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            399 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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=> D L4 7 IBIB ABS IND KWIC ED

L4   ANSWER 7 OF 134  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:206742  CAPLUS
DOCUMENT NUMBER:         144:439758
TITLE:                   Recrystallization of a Pharmaceutical Compound Using
                         Liquid and Supercritical Antisolvents
AUTHOR(S):               Park, Su-Jin; Jeon, Se-Yeoun; Yeo, Sang-Do
CORPORATE SOURCE:        Department of Chemical Engineering, Kyungpook National
                         University, Taegu, 702-701, S. Korea
SOURCE:                  Industrial & Engineering Chemistry Research (2006),
                         45(7), 2287-2293
                         CODEN: IECRED; ISSN: 0888-5885
PUBLISHER:               American Chemical Society
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Sulfabenzamide was recrystd. from its solns. by using liquid and
     supercrit. fluid as antisolvents.  The drug compound was dissolved
     in various organic solvents, such as acetone, methanol, ethanol,
     and Et acetate, and the solns. came into contact with two
     antisolvents, water (liquid) and carbon dioxide (supercrit. fluid).
     Variations of the habit, particle size, and the thermal behavior of the
     crystals were examined to investigate the effect of the operating
     temperature, type of solvent and antisolvent, mixing method,
     and the presence of ultrasound.  Crystal habits such as
     acicular, columnar, prismatic, equant, and tabular were obtained depending
     on the solvents and antisolvents used.  Larger
     crystals with a broader distribution were produced at higher
     temps., and crystal size was reduced when the solution was
     sonicated while precipitation occurred.  The variations of crystal size
     were correlated with the use of solubility parameters of solvents and
     antisolvents.  The thermal anal. of crystals revealed
     that the types of solvent and antisolvent employed in
     crystn. have influenced the internal structure of the resulting
     crystals and produced different polymorphs of
     sulfabenzamide.
CC   63-5 (Pharmaceuticals)
     Section cross-reference(s): 75
ST   sulfabenzamide recrystn
IT   Solvents
        (antisolvents; recrystn. of sulfabenzamide using liquid and supercrit.
        antisolvents)
IT   Solvents
        (organic; recrystn. of sulfabenzamide using liquid and supercrit.
        antisolvents)
IT   Crystal morphology
     Particle size
     Particle size distribution
       Polymorphism (crystal)
     Recrystallization
     Solubility
        (recrystn. of sulfabenzamide using liquid and supercrit.
        antisolvents)
IT   64-17-5, Ethanol, uses   67-56-1, Methanol, uses   67-64-1, Acetone, uses
     124-38-9, Carbon dioxide, uses   141-78-6, Ethyl acetate, uses
     7732-18-5, Water, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (recrystn. of sulfabenzamide using liquid and supercrit. antisolvents)
IT   127-71-9, Sulfabenzamide
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (recrystn. of sulfabenzamide using liquid and supercrit. antisolvents)
AB   Sulfabenzamide was recrystd. from its solns. by using liquid and
     supercrit. fluid as antisolvents.  The drug compound was dissolved
     in various organic solvents, such as acetone, methanol, ethanol,
     and Et acetate, and the solns. came into contact with two
     antisolvents, water (liquid) and carbon dioxide (supercrit. fluid).
     Variations of the habit, particle size, and the thermal behavior of the
     crystals were examined to investigate the effect of the operating
     temperature, type of solvent and antisolvent, mixing method,
     and the presence of ultrasound.  Crystal habits such as
     acicular, columnar, prismatic, equant, and tabular were obtained depending
     on the solvents and antisolvents used.  Larger
     crystals with a broader distribution were produced at higher
     temps., and crystal size was reduced when the solution was
     sonicated while precipitation occurred.  The variations of crystal size
     were correlated with the use of solubility parameters of solvents and
     antisolvents.  The thermal anal. of crystals revealed
     that the types of solvent and antisolvent employed in
     crystn. have influenced the internal structure of the resulting
     crystals and produced different polymorphs of
     sulfabenzamide.
IT   Crystal morphology
     Particle size
     Particle size distribution
       Polymorphism (crystal)
     Recrystallization
     Solubility
        (recrystn. of sulfabenzamide using liquid and supercrit.
        antisolvents)
ED   Entered STN:  08 Mar 2006
REFERENCE COUNT:         22    THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> D L4 25 IBIB ABS IND KWIC ED

L4   ANSWER 25 OF 134  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2003:641415  CAPLUS
DOCUMENT NUMBER:         139:372065
TITLE:                   A computer simulation based screening method for
                         crystallization processes
AUTHOR(S):               Thome, V.; Herrmann, M.; Pontius, H.; Kempa, P. B.;
                         Doerich, M.
CORPORATE SOURCE:        Fraunhofer Institut fuer Chemische Technologie,
                         Pfinztal, D-76327, Germany
SOURCE:                  International Annual Conference of ICT (2003), 34th,
                         103/1-103/8
                         CODEN: IACIEQ; ISSN: 0722-4087
PUBLISHER:               Fraunhofer-Institut fuer Chemische Technologie
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Crystn. of organic solids from solns. is often a difficult task
     because phase transitions, formation of solvates or complexation could
     occur.  Therefore it is important to find out solvent properties
     which have a pos. influence on the crystn. of desired
     polymorphs.  As it is material and time consuming to determine
     solvent properties by exptl. methods we used a SGI Octane
     workstation equipped with the program Cerius 4.2 (Accelrys) for calculating
     solvent by force field (cff 91 950-1.01) and semiempirical methods
     (WinMopac).  Moreover, a screening plan for the crystn. of
     nitramines was developed on the basis of 40 solvents,
     representing twelve different functional groups and the four influence
     factors: dipole moment, nonbond energy, molar volume and solvent
     polarity.  It's known that the electrostatic potential of a mol. surface
     is related to solvent properties like the H-bond donating
     parameter α and the H-bond acceptor parameter β.  It seems
     therefore necessary to include the electrostatic potential as an important
```

influence factor. Crystn. expts. were carried out with .vepsiln.-CL-20 in a automated crystn. device Quest from Argonaut. The recrystd. samples were analyzed by x-ray diffraction (XRD), SEM, and DSC to characterize occurring polymorphs, donor-acceptor complexes and morphologies of the crystals. We found high correlations between polymorphic phases and solvent properties. Furthermore models and concepts for solution mechanism, complexation or decompns. of CL-20 were developed. The results and systematic evaluation allowed us to predict further suitable solvents for the crystn. of .vepsiln.-CL-20.

CC 75-1 (Crystallography and Liquid Crystals)
Section cross-reference(s): 50

ST CL 20 explosive crystn computer simulation screening

IT Crystallization
Simulation and Modeling
Solvent effect
(computer simulation based screening method for crystallization processes)

IT Explosives
(computer simulation based screening method for crystallization processes applied to .vepsiln.-CL-20)

IT 135285-90-4, CL-20
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(computer simulation based screening method for crystallization processes applied to .vepsiln.-CL-20)

AB Crystn. of organic solids from solns. is often a difficult task because phase transitions, formation of solvates or complexation could occur. Therefore it is important to find out solvent properties which have a pos. influence on the crystn. of desired polymorphs. As it is material and time consuming to determine solvent properties by exptl. methods we used a SGI Octane workstation equipped with the program Cerius 4.2 (Accelrys) for calculating solvent by force field (cff 91 950-1.01) and semiempirical methods (WinMopac). Moreover, a screening plan for the crystn. of nitramines was developed on the basis of 40 solvents, representing twelve different functional groups and the four influence factors: dipole moment, nonbond energy, molar volume and solvent polarity. It's known that the electrostatic potential of a mol. surface is related to solvent properties like the H-bond donating parameter α and the H-bond acceptor parameter β. It seems therefore necessary to include the electrostatic potential as an important influence factor. Crystn. expts. were carried out with .vepsiln.-CL-20 in a automated crystn. device Quest from Argonaut. The recrystd. samples were analyzed by x-ray diffraction (XRD), SEM, and DSC to characterize occurring polymorphs, donor-acceptor complexes and morphologies of the crystals. We found high correlations between polymorphic phases and solvent properties. Furthermore models and concepts for solution mechanism, complexation or decompns. of CL-20 were developed. The results and systematic evaluation allowed us to predict further suitable solvents for the crystn. of .vepsiln.-CL-20.

ED Entered STN: 18 Aug 2003

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L4 42 IBIB ABS IND KWIC ED

L4 ANSWER 42 OF 134 CAPLUS

ACCESSION NUMBER: 2000:263770 CAPLUS
DOCUMENT NUMBER: 133:4293
TITLE: Polymorphism and pseudopolymorphism in organic crystals. A cambridge structural database study

AUTHOR(S): Sarma, Jagarlapudi A. R. P.; Desiraju, Gautam R.
CORPORATE SOURCE: Physical and Inorganic Chemistry Division, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

SOURCE: NATO ASI Series, Series C: Mathematical and Physical Sciences (1999), 539(Crystal Engineering: The Design and Application of Functional Solids), 325-356
CODEN: NSCSDW; ISSN: 0258-2023
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with .apprx.25 refs. An anal. with the Cambridge Structural Database (CSD) of polymorphism among single residue organic and organometallic entries reveals that the likelihood of the phenomenon is low and more significantly, does not vary with the C content of the mol. in the range C1 to C80. Larger mols. with a larger number of potential recognition sites during crystn. also cascade into their stable crystal structures more efficiently than do smaller mols. In effect, polymorphism is fat less of a problem in crystal engineering and related disciplines than was held previously. Compds. that contain conformationally flexible groups which can also form strong H bonds, for example -OH and -NH2 are more likely to occur in polymorphic forms. A description of polymorphism in terms of patterns of similar or dissimilar supramol. synthons is also given. Polymorphism occurs when the same synthon can be constructed in different ways. This can happen when there are multiple occurrences of the same functional group in a mol. The phenomenon of pseudopolymorphism also was examined with the CSD. The inclusion of H2O in organic crystals is especially common while CH2Cl2 is included in organometallics. Other H bonding solvents like DMSO, DMF and dioxane are also included frequently. When the occurrence of pseudopolymorphism is corrected for solvent usage, it appears that EtOH and hexane occur in crystals far less than their usage as recrystn. solvents might indicate. Certain compds. like resorcinol, pyrazine-2-carboxamide and N-2-thiazolylsulfanilamide show strikingly different polymorphic forms. Yet, in the end, polymorphism is essentially a random phenomenon and only certain combinations of mol. size, shape and functionality, or in a supramol. sense, a particular flexibility in synthon construction can lead to its occurrence.

CC 22-0 (Physical Organic Chemistry)
Section cross-reference(s): 75

ST review polymorphism pseudopolymorphism org crystal cambridge database

IT Polymorphism (crystal)
(cambridge structural database study of polymorphism and pseudopolymorphism in organic crystals)

IT Crystals
(organic; cambridge structural database study of polymorphism and pseudopolymorphism in organic crystals)

AB A review, with .apprx.25 refs. An anal. with the Cambridge Structural Database (CSD) of polymorphism among single residue organic and organometallic entries reveals that the likelihood of the phenomenon is low and more significantly, does not vary with the C content of the mol. in the range C1 to C80. Larger mols. with a larger number of potential recognition sites during crystn. also cascade into their stable crystal structures more efficiently than do smaller mols. In effect, polymorphism is fat less of a problem in crystal engineering and related disciplines than was held previously. Compds. that contain conformationally flexible groups which can also form strong H bonds, for example -OH and -NH2 are more likely to occur in polymorphic forms. A description of polymorphism in terms of patterns of similar or dissimilar supramol. synthons is also given. Polymorphism occurs when the same synthon can be constructed in different ways. This can happen when there are multiple occurrences of the same functional group in a mol. The phenomenon of

pseudopolymorphism also was examined with the CSD. The inclusion of H_2O in organic crystals is especially common while CH_2Cl_2 is included in organometallics. Other H bonding solvents like DMSO, DMF and dioxane are also included frequently. When the occurrence of pseudopolymorphism is corrected for solvent usage, it appears that EtOH and hexane occur in crystals far less than their usage as recrystn. solvents might indicate. Certain compds. like resorcinol, pyrazine-2-carboxamide and N-2-thiazolylsulfanilamide show strikingly different polymorphic forms. Yet, in the end, polymorphism is essentially a random phenomenon and only certain combinations of mol. size, shape and functionality, or in a supramol. sense, a particular flexibility in synthon construction can lead to its occurrence.

ED Entered STN: 24 Apr 2000
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 12 IBIB ABS IND KWIC ED

L9 ANSWER 12 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:953414 CAPLUS
DOCUMENT NUMBER: 143:311634
TITLE: Molecular interactions between solvent and pharmaceutical compounds in crystallization of polymorphic systems
AUTHOR(S): Mirmehrabi, Mahmoud; Rohani, Sohrab
CORPORATE SOURCE: Chemical and Biochemical Engineering Department, The University of Western Ontario, London, ON, N6A 5B9, Can.
SOURCE: AIChE Annual Meeting, Conference Proceedings, Austin, TX, United States, Nov. 7-12, 2004 (2004), 230B/1-230B/4. American Institute of Chemical Engineers: New York, N. Y.
CODEN: 69GSKT; ISBN: 0-8169-0965-2
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English

AB Polymorphism in pharmaceutical solids is a major issue that has medical, financial and legal implications. There are many thermodn. and kinetics factors which affect the polymorph selectivity during the crystallization process such as nucleation temperature, supersatn. and type of solvent. Among these parameters, type of solvent is a major kinetic factor that has drawn the attention of researchers. Literature is ripe with research showing the effect of solvent on the polymorph selectivity, mainly using the polar and non-polar terminol., but seldom the researchers have explained the effect of solvent at mol. level. This work looks into the effect of solvent and the corresponding intermol. interactions on the polymorphic selectivity. Two case studies on the effect of solvent will be discussed for polymorphic systems of stearic acid (used for tablet coating) and ranitidine hydrochloride (H2-receptor antagonist drug).

CC 63-5 (Pharmaceuticals)
ST stearic acid ranitidine hydrochloride polymorphism crystn solvent effect
IT Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
(mol. interactions between solvent and pharmaceutical compds. in crystn. of polymorphic systems)
IT 57-11-4, Stearic acid, biological studies 66357-59-3, Ranitidine hydrochloride
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mol. interactions between solvent and pharmaceutical compds. in crystallization of polymorphic systems)
IT Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
(mol. interactions between solvent and pharmaceutical compds. in crystn. of polymorphic systems)
ED Entered STN: 01 Sep 2005
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 17 IBIB ABS IND KWIC ED

L9 ANSWER 17 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:574862 CAPLUS
DOCUMENT NUMBER: 144:27234
TITLE: An approach to solvent screening for crystallization of polymorphic pharmaceuticals and fine chemicals
AUTHOR(S): Mirmehrabi, Mahmoud; Rohani, Sohrab
CORPORATE SOURCE: Chemical and Biochemical Engineering Department, The University of Western Ontario, London, ON, N6A 5B9, Can.
SOURCE: Journal of Pharmaceutical Sciences (2005), 94(7), 1560-1576
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is desirable to have a systematic approach for predicting or interpreting the effect of the solvents on the production of polymorphs. A method based on the atomic electronegativity is suggested that calcs. the partial charge distribution in the solute and solvent mols. Using the calculated partial charges, correlations are developed to predict the hydrogen bonding ability of the solute and/or solvent mols. The predictive capability of the proposed correlations is compared with the results of a quantum mechanics approach. Selection of the right solvent may play a significant role in the formation of a desirable polymorph or solvate. The most important properties of class 2 and 3 solvents of International Conference on Harmonization (ICH) for crystallization of polymorphic compds. are listed in this paper. The partial charge calcn. has been used as a tool for analyzing the solvent impact on polymorphic isolation of two compds.: ranitidine hydrochloride (H2 receptor antagonist) and stearic acid (used as excipients or in coating the tablets).

CC 63-5 (Pharmaceuticals)
ST ranitidine stearate crystn polymorphism solvent
IT Crystal structure
Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
Solvents
(approach to solvent screening for crystn. of polymorphic pharmaceuticals and fine chems.)
IT 60-29-7, Ethyl Ether, properties 64-17-5, Ethanol, properties 64-18-6, Formic acid, properties 64-19-7, Acetic acid, properties 65-85-0, Benzoic acid, properties 67-56-1, Methanol, properties 67-63-0, Isopropanol, properties 67-64-1, Acetone, properties 67-66-3, Chloroform, properties 67-68-5, Dimethyl sulfoxide, properties 68-12-2, Dimethylformamide, properties 70-55-3, Toluene-p-sulfonamide 71-23-8, n-Propanol, properties 71-36-3, 1-Butanol, properties 71-41-0, 1-Pentanol, properties 75-05-8, Acetonitrile, properties

75-09-2, Dichloromethane, properties 75-12-7, Formamide, properties
75-31-0, Isopropylamine, properties 75-52-5, Nitromethane, properties
75-65-0, tert-Butyl alcohol, properties 75-89-8, 2,2,2-Trifluoroethanol
75-97-8 75-98-9, Pivalic Acid 76-05-1, Trifluoroacetic Acid,
properties 78-40-0, Triethyl Phosphate 78-83-1, 2-Methyl-1-propanol,
properties 78-92-2, 2-Butanol 78-93-3, Methyl Ethyl Ketone, properties
79-01-6, properties 79-20-9, Methyl Acetate 88-18-6, 2-tert-Butyl
Phenol 91-21-4, 1,2,3,4-Tetrahydro Isoquinoline 95-16-9, Benzothiazole
95-47-6, o-Xylene, properties 95-48-7, 2-Methyl Phenol, properties
95-57-8, 2-Chlorophenol 96-48-0, γ-Butyrolactone 98-82-8, Cumene
98-86-2, Acetophenone, properties 99-07-0, 3-N,N,Dimethylaminophenol
100-02-7, 4-Nitrophenol, properties 100-15-2, 4-Nitro-N-Methylaniline
100-46-9, Benzylamine, properties 100-47-0, Benzonitrile, properties
100-51-6, Benzyl alcohol, properties 100-54-9, 3-Cyanopyridine
100-66-3, Anisole, properties 100-70-9, 2-Cyanopyridine 103-84-4,
Acetanilide 106-42-3, p-Xylene, properties 107-07-3, 2-Chloroethanol,
properties 107-11-9, Allylamine 107-14-2 107-21-1, Ethylene glycol,
properties 107-87-9, 2-Pentanone 108-10-1, Methyl isobutyl Ketone
108-21-4, Isopropyl Acetate 108-38-3, m-Xylene, properties 108-39-4,
3-Methyl Phenol, properties 108-43-0, 3-Chlorophenol 108-87-2, Methyl
Cyclohexane 108-88-3, Toluene, properties 108-89-4, 4-Methylpyridine
108-90-7, Chlorobenzene, properties 108-94-1, Cyclohexanone, properties
108-95-2, Phenol, properties 108-99-6, 3-Methylpyridine 109-09-1,
2-Chloropyridine 109-60-4, Propyl Acetate 109-66-0, n-Pentane,
properties 109-86-4, 2-Methoxyethanol 109-94-4, Ethyl Formate
109-97-7, Pyrrole 109-99-9, Tetrahydrofuran, properties 110-19-0,
Isobutyl Acetate 110-54-3, n-Hexane, properties 110-71-4,
1,2-Dimethoxyethane 110-80-5, 2-Ethoxyethanol 110-82-7, Cyclohexane,
properties 110-86-1, Pyridine, properties 111-27-3, 1-Hexanol,
properties 119-64-2, Tetralin 120-72-9, Indole, properties 123-51-3,
3-Methyl-1-Butanol 123-86-4, Butyl Acetate 123-91-1, 1,4-Dioxane,
properties 126-33-0, Sulfolane 127-19-5, N,N-Dimethylacetamide
136-95-8, 2-Aminobenzothiazole 141-78-6, Ethyl acetate, properties
142-82-5, Heptane, properties 142-96-1, Dibutyl ether 150-76-5,
4-Methoxyphenol 156-59-2 156-60-5 288-14-2, Isoxazole 288-42-6,
Oxazole 288-47-1, Thiazole 354-38-1, 2,2,2-Trifluoroacetamide
372-47-4, 3-Fluoropyridine 372-48-5, 2-Fluoropyridine 393-12-4
402-45-9, 4-Trifluoromethylphenol 407-24-9 494-19-9 563-80-4, Methyl
isopropyl Ketone 565-80-0, Diisopropyl Ketone 583-58-4,
3,4-Dimethylpyridine 591-78-6, Methyl butyl Ketone 611-20-1,
2-Cyanophenol 611-74-5 616-47-7, 1-Methylimidazole 617-84-5,
Diethylformamide 617-94-7, 2-Phenyl-2-propanol 620-08-6,
4-Methoxypyridine 623-03-0, 4-Chlorobenzonitrile 626-55-1,
3-Bromopyridine 626-60-8, 3-Chloropyridine 632-22-4, Tetramethylurea
637-53-6, Thioacetanilide 646-06-0, 1,3-Dioxolane 712-33-4 753-90-2
771-61-9, Pentafluorophenol 791-28-6, Triphenylphosphine Oxide
874-90-8, 4-Methoxybenzonitrile 920-66-1, 1,1,1,3,3,3-Hexafluoro-2-propanol 930-36-9, 1-Methylpyrazole 930-88-1, N-Methylmaleimide
1003-10-7, Dihydro-2(3H)-Thiophenone 1122-58-3 1123-85-9,
2-Phenyl-1-propanol 1576-37-0, N-Benzyl-p-Toluenesulfonamide
1628-89-3, 2-Methoxypyridine 1634-04-4, tert-Butyl Methyl Ether
5326-57-8 6830-83-7 6876-73-9 6969-90-0 13130-15-9 14278-35-4
15980-15-1, 1,4-Thioxane 18039-42-4 19727-83-4 20662-84-4,
2,4,5-Trimethyloxazole 30207-69-3, Methylpyrrolidinone 40964-54-3
42060-55-9 53374-49-5 95728-77-1 111452-17-6 126379-88-2
126379-91-7 126379-94-0 126379-95-1
RL: PRP (Properties)
(approach to solvent screening for crystallization of polymorphic pharmaceuticals and fine chems.)

IT 57-11-4, Stearic acid, biological studies 66357-59-3, Ranitidine hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(approach to solvent screening for crystallization of polymorphic pharmaceuticals and fine chems.)

IT Crystal structure
Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
Solvents
(approach to solvent screening for crystn. of polymorphic pharmaceuticals and fine chems.)

ED Entered STN: 04 Jul 2005

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 48 IBIB ABS IND KWIC ED

L9 ANSWER 48 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:564320 CAPLUS
DOCUMENT NUMBER: 140:133465
TITLE: Crystallization of molecules. Consequences in terms of polymorphism and application in pharmaceutics. Basic concepts
AUTHOR(S): Bauer, M.
CORPORATE SOURCE: Departement international d'analyse, Sanofi Synthelabo Recherche, Toulouse, 31036, Fr.
SOURCE: S.T.P. Pharma Pratiques (2003), 13(2), 47-61
CODEN: SPPRER; ISSN: 1157-1497
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review. In this article, a brief description of the crystallization process is provided as well as definitions regarding polymorphism, pseudo-polymorphism and crystalline habit. After having recalled some basic aspects of physics and thermodn. of polymorphism and pseudo-polymorphism, the article discusses several examples: the strategy of cryst. form selection of a new chemical entity currently studied in clin. trials; the impact of the agglomeration/aggregation states of furosemide on the dissoln. of the corresponding tablets; the example of the taltireline crystn. taken from literature and investigating the impact of different parameters (in particular residual solvents) on the crystn. control. A brief introduction to the amorphous phases and their potential applications in the pharmaceutical domain is tackled as well as some regulatory considerations.

CC 63-0 (Pharmaceuticals)

ST review crystn polymorphism pharmaceutical

IT Crystallization
Drugs
Polymorphism (crystal)
(crystallization of mols. consequences in terms of polymorphism and application in pharmaceutics)

AB A review. In this article, a brief description of the crystallization process is provided as well as definitions regarding polymorphism, pseudo-polymorphism and crystalline habit. After having recalled some basic aspects of physics and thermodn. of polymorphism and pseudo-polymorphism, the article discusses several examples: the strategy of cryst. form selection of a new chemical entity currently studied in clin. trials; the impact of the agglomeration/aggregation states of furosemide on the dissoln. of the corresponding tablets; the example of the taltireline crystn. taken from literature and investigating the impact of different parameters (in particular residual

solvents) on the crystn. control. A brief introduction
to the amorphous phases and their potential applications in the
pharmaceutical domain is tackled as well as some regulatory
considerations.

ED Entered STN: 24 Jul 2003
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 51 IBIB ABS IND KWIC ED

L9 ANSWER 51 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:107138 CAPLUS
DOCUMENT NUMBER: 138:262829
TITLE: Toward Stereochemical Control, Monitoring, and Understanding of Crystal Nucleation
AUTHOR(S): Weissbuch, Isabelle; Lahav, Meir; Leiserowitz, Leslie
CORPORATE SOURCE: Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot, 76100, Israel
SOURCE: Crystal Growth & Design (2003), 3(2), 125-150
CODEN: CGDEFU; ISSN: 1528-7483
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB In this review, the delicate interplay between stereochem. control, monitoring at the subnanometer level, and an understanding of crystal nucleation is probed. Control of crystal nucleation may be achieved employing tailor-made auxiliaries, which are either nucleation inhibitors or promoters. The process may be monitored at an interface via grazing incidence x-ray diffraction (GIXD). By these means, the authors can glean exptl. knowledge of crystal nucleation in various mol. systems. A hypothesis was invoked that supersatd. solns. containing mol. clusters adopt various arrangements and shapes, some of which resemble the crystals into which they develop. This hypothesis was taken advantage of for the design of tailored inhibitors in achieving kinetic resolution of enantiomers and induced precipitation of particular crystal polymorphs. The control and behavior of polymorphic crystn. may be understood at the mol. level through the interplay between inhibitor, solvent, solute, and the surface layer crystal structures. With respect to promotion of crystal nucleation, it may be achieved by Langmuir monolayers at the air-aqueous solution interface, acting as a templating agent. Determination of the monolayer crystal structure by GIXD yields the extent and nature of the complementary fit between nucleator and nucleant. Finally, GIXD was applied to monitor by a snapshot technique the layer-by-layer crystalline assembly of cholesterol mols. at the air-H2O interface, which involved changes in mol. packing as the film grew in thickness.

CC 75-0 (Crystallography and Liquid Crystals)
ST review stereochem control monitoring understanding crystal nucleation
IT Crystallization
Polymorphism (crystal)
(control and behavior of polymorphic crystallization)
IT Langmuir monolayers
(in understanding of crystal nucleation)
IT Crystal nucleation
Stereochemistry
(toward stereochem. control, monitoring, and understanding of crystal nucleation)
AB . . . supersatd. solns. containing mol. clusters adopt various arrangements and shapes, some of which resemble the crystals into which they develop. This hypothesis was taken advantage of for the design of tailored inhibitors in achieving kinetic resolution of enantiomers and induced precipitation of particular crystal polymorphs. The control and behavior of polymorphic crystn. may be understood at the mol. level through the interplay between inhibitor, solvent, solute, and the surface layer crystal structures. With respect to promotion of crystal nucleation, it may be achieved by Langmuir monolayers at the air-aqueous solution interface, acting as a templating agent. Determination of the monolayer crystal structure by GIXD yields the extent and nature of the complementary fit between nucleator and nucleant. Finally, GIXD was applied. . .

ED Entered STN: 12 Feb 2003
REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 61 IBIB ABS IND KWIC ED

L9 ANSWER 61 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:41527 CAPLUS
DOCUMENT NUMBER: 136:202341
TITLE: Control of solvent-mediated transformation of crystal polymorphs using a newly developed batch crystallizer (WWDJ-crystallizer)
AUTHOR(S): Shan, Gu; Igarashi, Koichi; Noda, Hideo; Ooshima, Hiroshi
CORPORATE SOURCE: Department of Bioapplied Chemistry, Osaka City University, Sumiyoshi-ku, Osaka, 558-8585, Japan
SOURCE: Chemical Engineering Journal (Amsterdam, Netherlands) (2002), 85(2-3), 169-176
CODEN: CMEJAJ; ISSN: 1385-8947
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a newly developed batch crystallizer (WWDJ-crystallizer) equipped with a slurry sprinkler named Wall Wetter and a double-deck jacket, a suppression of the solvent-mediated transformation of the metastable polymorphic crystals was attempted. Crystallization of l-glutamic acid was carried out to show an example of the suppression. The target polymorphic crystals, the metastable α-form crystals were exclusively obtained from the aqueous solution without transformation to the stable β-form polymorph even at a temperature where the transformation could not be avoided if a conventional batch crystallizer was used. The characteristic size of crystals obtained by WWDJ-crystallizer was large and their size distribution was narrow, comparing with those obtained by a conventional crystallizer.

CC 48-1 (Unit Operations and Processes)
Section cross-reference(s): 34, 45, 75
ST solvent transformation crystal polymorph batch crystallizer WWDJ
IT Crystallization
(batch; control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)
IT Crystallization apparatus
Crystallization temperature
Particle size distribution
Polymorphism (crystal)
(control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)
IT 56-86-0P, L-Glutamic acid, processes
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)

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      (control of solvent-mediated transformation of crystal polymorphs using
      newly developed batch crystallizer)
IT   Crystallization
      (batch; control of solvent-mediated transformation of
      crystal polymorphs using newly developed batch
      crystallizer)
IT   Crystallization apparatus
       Crystallization temperature
     Particle size distribution
     Polymorphism (crystal)
      (control of solvent-mediated transformation of
      crystal polymorphs using newly developed batch
      crystallizer)
ED   Entered STN:  16 Jan 2002
REFERENCE COUNT:        16    THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> D L9 67 IBIB ABS IND KWIC ED

L9   ANSWER 67 OF 93  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       2000:662268  CAPLUS
DOCUMENT NUMBER:        133:195206
TITLE:                  Crystallisation of Polymorphs: Thermodynamic Insight
                        into the Role of Solvent
AUTHOR(S):              Threlfall, Terry
CORPORATE SOURCE:       Chemistry Department, University of York, Heslington
                        York, YO10 5DD, UK
SOURCE:                 Organic Process Research & Development (2000), 4(5),
                        384-390
                        CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER:              American Chemical Society
DOCUMENT TYPE:          Journal
LANGUAGE:               English
AB   Dependent on the conditions, crystallization of polymorphs from solvent can be
     under kinetic or thermodn. control.  In the latter case the nature of the
     solvent is immaterial in respect of the polymorph produced.  The
     conditions under which each of these factors may apply are analyzed in
     detail.  The transition point between two dimorphs may not present a sharp
     divide in which crystallization above and below the transition temperature
produces the
     high melting and the low melting polymorph, resp.  It is shown that even
     in those cases where the choice of solvent appears to be critical this may be
     a secondary effect related to the concentration attainable in that solvent at a
     certain temperature rather than a specific effect dependent on solvent-solute
     interaction.  A corollary to these considerations is the necessity to determine
     solubility curves and metastable zone widths in order to be able to control
     polymorph crystallization
CC   48-1 (Unit Operations and Processes)
     Section cross-reference(s): 69
ST   crystn polymorph solvent thermodn
IT   Crystallization
       Polymorphism (crystal)
     Solvents
     Thermodynamics
        (thermodn. insight into role of solvent in crystn.
        of polymorphs)
IT   Crystallization
       Polymorphism (crystal)
     Solvents
     Thermodynamics
        (thermodn. insight into role of solvent in crystn.
        of polymorphs)
ED   Entered STN:  22 Sep 2000

REFERENCE COUNT:        18    THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> D L9 77 IBIB ABS IND KWIC ED

L9   ANSWER 77 OF 93  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       1997:477003  CAPLUS
DOCUMENT NUMBER:        127:150362
TITLE:                  Crystal science techniques in the manufacture of
                        chiral compounds
AUTHOR(S):              Wood, W. M. L.
CORPORATE SOURCE:       ZENECA Huddersfield Works, Huddersfield, UK
SOURCE:                 Chirality in Industry II (1997), 119-156.  Editor(s):
                        Collins, Andrew N.; Sheldrake, G. N.; Crosby, J.
                        Wiley: Chichester, UK.
                        CODEN: 64TBAW
DOCUMENT TYPE:          Conference; General Review
LANGUAGE:               English
AB   A review, with 29 refs., on application of crystallization principles to
     large-scale production of chiral compds.  Crystal,
     polymorphs and solvates, and crystal habits and
     modifiers; crystn. processes [supersatn., solvent
     choice, solubility curves, nucleation and crystal size control]; and
     isolation of metastable phases are discussed.  Separation of enantiomers by
     diastereoisomer formation, separation of diastereoisomers, and resolution by
     direct crystallization of enantiomers, are also discussed.
CC   45-0 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
     Section cross-reference(s): 75
ST   review crystn process chiral compd manuf; supersatn soly crystn control
     review; enantiomer sepn crystn review
IT   Crystal morphology
     Crystallization
     Diastereomers
     Resolution (separation)
     Supersaturation
        (crystallization principles and processes in manufacture of chiral compds.)
AB   A review, with 29 refs., on application of crystallization principles to
     large-scale production of chiral compds.  Crystal,
     polymorphs and solvates, and crystal habits and
     modifiers; crystn. processes [supersatn., solvent
     choice, solubility curves, nucleation and crystal size control]; and
     isolation of metastable phases are discussed.  Separation of enantiomers by
     diastereoisomer formation, separation of diastereoisomers, and resolution by
     direct crystallization of enantiomers, are also discussed.
ED   Entered STN:  31 Jul 1997


=> D L9 79 IBIB ABS IND KWIC ED

L9   ANSWER 79 OF 93  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       1997:55240  CAPLUS
DOCUMENT NUMBER:        126:148257
TITLE:                  Crystallization behavior and functionalities of
                        pharmaceutical and food materials
AUTHOR(S):              Yamamoto, Hideji
CORPORATE SOURCE:       Dep. Food Sci. & Technology, Faculty Engin., Fukuyama
                        Univ., Fukuyama, 729-02, Japan
SOURCE:                 Nippon Kessho Seicho Gakkaishi (1996), 23(5), 422-429
                        CODEN: NKSGDK; ISSN: 0385-6275
PUBLISHER:              Nippon Kessho Seicho Gakkai
DOCUMENT TYPE:          Journal; General Review
LANGUAGE:               Japanese
AB   A review with 44 refs.  This article reviews recent studies on the
crystallization
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     phenomena and operation for the preparation of pharmaceuticals and functional
     foods.  Main interests are focused on selective crystn. of
     polymorphs and solvent mediated phase transition,
     clathrative crystn. of green tea polyphenol with cyclodextrin,
     crystn. of maltose accompanying anomerization process,
     crystallinity and functionalities of drug, and the modification of
     crystal habits by controlling agitation condition for improvement
     of separation by filtration.
CC   63-0 (Pharmaceuticals)
ST   review crystn pharmaceutical food
IT   Crystallization
     Drug delivery systems
     Food
        (crystallization behavior and functionalities of pharmaceutical and food
        materials)
AB   A review with 44 refs.  This article reviews recent studies on the
crystallization
     phenomena and operation for the preparation of pharmaceuticals and functional
     foods.  Main interests are focused on selective crystn. of
     polymorphs and solvent mediated phase transition,
     clathrative crystn. of green tea polyphenol with cyclodextrin,
     crystn. of maltose accompanying anomerization process,
     crystallinity and functionalities of drug, and the modification of
     crystal habits by controlling agitation condition for improvement
     of separation by filtration.
ED   Entered STN:  25 Jan 1997


=> D L9 80 IBIB ABS IND KWIC ED

L9   ANSWER 80 OF 93  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1996:127536  CAPLUS
DOCUMENT NUMBER:          124:246838
TITLE:                    Interactions in molecular crystals. Part 85.
                          Solvent-shared radical ion pairs
                          [pyrene•-Na+O(C2H5)2]∞: ESR evidence for two
                          different aggregates in solution, room temperature
                          crystallization, and structural proof of
                          another polymorphic modification
AUTHOR(S):                Naether, Christian; Bock, Hans; Claridge, Rodney F. C.
CORPORATE SOURCE:         Inst. Inorg. Chem., Johann Wolfgang Goethe Univ.
                          Frankfurt, Frankfurt, D-60439, Germany
SOURCE:                   Helvetica Chimica Acta (1996), 79(1), 84-91
                          CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER:                Verlag Helvetica Chimica Acta
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   The reduction of pyrene with Na in aprotic diethylether allows to crystallize
     the extremely air-sensitive radical ion pair pyrene-Na-diethylether.  The
     single crystal structure determination at 130 K shows that each Na counter
cation,
     solvated by one diethylether mol., is η3- and η6-coordinated to 1
     of the short-axis 6-membered rings of 2 pyrene radical anions.  The
     resulting dibenzene-Na sandwiches form a string, in which the hydrocarbon
     planes are canted to each other by 62°.  In the pyrene
     radical-anion skeleton, no distortion due to its neg. charge can be
     detected relative to that of the neutral mol.  From the temperature-dependent
     signal multiplets of preceding ESR investigations, the solvent-separated
     pyrene radical anion, and 2 different contact radical-ion pairs were
     identified and their structures in solution approximated by potential-energy
     ests.  Referring to the recently discovered long-axis Na+ contact ion pair
     polymorph, crystallized at lower temps., the structure reported here represents
     the 2nd and probably thermodynamically more stable one.  Both the ESR and
     the structural results provide some insight into the multidimensional
     networks of equilibrium in aprotic solution, which are activated by alkali
metal
     reduction of unsatd. organic compds.
CC   75-8 (Crystallography and Liquid Crystals)
ST   crystn mol structure pyrene sodium ethylether
IT   Crystal structure
     Crystallization
     Molecular structure
        (of pyrene sodium diethylether radical ion pairs)
IT   174878-16-1, properties
     RL: PEP (Physical, engineering or chemical process); PRP (Properties);
     PROC (Process)
        (crystallization and crystal structure of)
TI   Interactions in molecular crystals. Part 85. Solvent
     -shared radical ion pairs [pyrene•-Na+O(C2H5)2]∞: ESR evidence
     for two different aggregates in solution, room temperature
     crystallization, and structural proof of another
     polymorphic modification
ED   Entered STN:  01 Mar 1996


=> D L9 83 IBIB ABS IND KWIC ED

L9   ANSWER 83 OF 93  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1995:510762  CAPLUS
DOCUMENT NUMBER:          122:252333
TITLE:                    Understanding and control of nucleation, growth,
                          habit, dissolution and structure of two- and
                          three-dimensional crystals using 'tailor-made'
                          auxiliaries
AUTHOR(S):                Weissbuch, Isabelle; Popovitz-Biro, Ronit; Lahav,
                          Meir; Leiserowitz, Leslie
CORPORATE SOURCE:         Dep. Mater. Interfaces, Weizmann Inst. Sci., Rehovot,
                          76100, Israel
SOURCE:                   Acta Crystallographica, Section B: Structural Science
                          (1995), B51(2), 115-48
                          CODEN: ASBSDK; ISSN: 0108-7681
PUBLISHER:                Munksgaard
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review, with many refs.  Tailor-made auxiliaries for the control of
     nucleation and growth of mol. crystals may be classified into two broad
     categories: inhibitors and promoters.  Tailor-made inhibitors of
     crystal growth can be used for a variety of purposes, which
     include morphol. engineering and etching, reduction of crystal
     symmetry, assignment of absolute structure of chiral mols. and polar
     crystals, elucidation of the effect of solvent on
     crystal growth, and crystn. of a desired
     polymorph.  As for crystal growth promoters, monolayers of
     amphiphilic mols. on H2O were used to induce the growth of a variety of
     three-dimensional crystals at the monolayer-solution interface by structural
     match, mol. complementarity or electrostatic interaction.  A particular
     focus is made on the induced nucleation of ice by monolayers of H2O-insol.
     aliphatic alcs.  The two-dimensional crystalline structures of such monolayers
     were studied by grazing incidence x-ray diffraction.  It has become
     possible to monitor, by this method, the growth, dissoln. and structure of
     self-aggregated crystalline monolayers, and indeed multilayers, affected by the
     interaction of solvent mols. in the aqueous subphase with the amphiphilic
     headgroups, and using tailor-made amphiphilic additives.
CC   75-0 (Crystallography and Liquid Crystals)
ST   review nucleation growth morphol structure crystal; dissoln crystal review
IT   Crystal growth
     Crystal morphology
     Crystal nucleation
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Crystal structure
Solution process
(understanding and control of nucleation, growth, habit, dissoln. and structure of two- and three-dimensional crystals using tailor-made auxiliaries)

AB A review, with many refs. Tailor-made auxiliaries for the control of nucleation and growth of mol. crystals may be classified into two broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes, which include morphol. engineering and etching, reduction of crystal symmetry, assignment of absolute structure of chiral mols. and polar crystals, elucidation of the effect of solvent on crystal growth, and crystn. of a desired polymorph. As for crystal growth promoters, monolayers of amphiphilic mols. on H2O were used to induce the growth of a variety of three-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or electrostatic interaction. A particular focus is made on the induced nucleation of ice by monolayers of H2O-insol.. . .

ED Entered STN: 26 Apr 1995

=> D L9 84 IBIB ABS IND KWIC ED

L9 ANSWER 84 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1994:19392 CAPLUS
DOCUMENT NUMBER:	120:19392
TITLE:	Tailor-made auxiliaries for the control of nucleation, growth and dissolution of two- and three-dimensional crystals
AUTHOR(S):	Lahav, M.; Leiserowitz, L.
CORPORATE SOURCE:	Dep. Mater. Interfaces, Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE:	Journal of Physics D: Applied Physics (1993), 26(8B), B22-B31 CODEN: JPAPBE; ISSN: 0022-3727
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review with 51 refs. Tailor-made mol. auxiliaries for the control of nucleation and growth of mol. crystals may be classified into 2 broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes which include morphol. engineering, reduction of crystal symmetry, assignment of absolute structure of polar crystals, elucidation of the effect of solvent on crystal growth and crystn. of a desired polymorph. As for crystal growth promoters, Langmuir monolayers on water have been used to induce growth of 3-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or an electrostatic interaction. The 2-dimensional crystalline structures of these monolayers have been studied by grazing-incidence x-ray diffraction (GIXD). It has become possible to monitor, by GIXD, the growth and dissoln. of self-aggregated crystalline monolayers affected by the interaction of solvent mols. in the aqueous subphase with the monolayer headgroups.

CC 75-0 (Crystallography and Liquid Crystals)

ST review crystal nucleation growth dissoln inhibitor; promoter crystal nucleation growth dissoln review; nucleation crystal inhibitor promoter review; growth crystal inhibitor promoter review; dissoln crystal inhibitor promoter review

IT Crystal growth
Crystal nucleation
Crystallization
Solution process
(of two- and three-dimensional mol. crystals, tailor-made inhibitors and promoters for)

IT Solvent effect
(on crystal growth and crystn. of polymorphs)

AB A review with 51 refs. Tailor-made mol. auxiliaries for the control of nucleation and growth of mol. crystals may be classified into 2 broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes which include morphol. engineering, reduction of crystal symmetry, assignment of absolute structure of polar crystals, elucidation of the effect of solvent on crystal growth and crystn. of a desired polymorph. As for crystal growth promoters, Langmuir monolayers on water have been used to induce growth of 3-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or an electrostatic interaction. The 2-dimensional crystalline structures of these monolayers have been studied by grazing-incidence x-ray diffraction (GIXD). It has become possible. . .

IT Solvent effect
(on crystal growth and crystn. of polymorphs)

ED Entered STN: 08 Jan 1994

=> D L18 18 33 43 66 73 78 90 108 118 124 134 148 163 164 172 179 185 206 211 216
245 259 268 289 298 348 377 378 433 IBIB ABS IND KWIC ED

L18 ANSWER 18 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:235740 CAPLUS
DOCUMENT NUMBER: 145:62420
TITLE: Preferential enrichment: significant influence of minor molecular modification on the mode of polymorphic transition during crystallization
AUTHOR(S): Fujimoto, Daisuke; Takahashi, Hiroki; Ariga, Tomomi; Tamura, Rui
CORPORATE SOURCE: Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan
SOURCE: Chirality (2006), 18(3), 188-195
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relationship between the mol. structure and the occurrence of Preferential Enrichment, an unusually symmetry-breaking enantiomeric resolution phenomenon observed upon simple recrystn. of a certain kind of racemic crystals from organic solvents, has been investigated with respect to a new series of racemic ammonium sulfonate compds. Racemic [2-[4-(3-ethoxy-2-hydroxypropoxy)phenylcarbamoyl]ethyl]trimethylammonium p-iodobenzenesulfonate [(±)-1a] can show preferential enrichment by simple recrystn. from EtOH, whereas its terminal methoxy and propoxy derivs. [(±)-1b and (±)-1c] are unable to do so. The influence of such a minor mol. modification on Preferential Enrichment has been rationalized in terms of the change of the mode of polymorphic transition during crystn., which has been confirmed by in situ ATR-FTIR (ReactIR) spectroscopy in solution and in the solid state and by X-ray crystallog. anal. of their single crystals.

CC 22-3 (Physical Organic Chemistry)
Section cross-reference(s): 75
ST preferential optical enrichment polymorphic transition crystn
IT IR reflectance spectroscopy
(attenuated total; preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)
IT Resolution (separation)
(enantiomeric; preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)
IT Crystal structure
Polymorphism (crystal)
Recrystallization
Structural phase transition
(preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)
IT 891786-96-2P 891786-98-4P 891786-99-5P
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)
IT 891787-00-1P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)
IT 215030-54-9 494847-23-3 891787-01-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preferential enrichment: significant influence of minor mol. modification on the mode of polymorphic transition during crystallization)

AB The relationship between the mol. structure and the occurrence of Preferential Enrichment, an unusually symmetry-breaking enantiomeric resolution phenomenon observed upon simple recrystn. of a certain kind of racemic crystals from organic solvents, has been investigated with respect to a new series of racemic ammonium sulfonate compds. Racemic [2-[4-(3-ethoxy-2-hydroxypropoxy)phenylcarbamoyl]ethyl]trimethylammonium p-iodobenzenesulfonate [(±)-1a] can show preferential enrichment by simple recrystn. from EtOH, whereas its terminal methoxy and propoxy derivs. [(±)-1b and (±)-1c] are unable to do so. The influence of such a minor mol. modification on Preferential Enrichment has been rationalized in terms of the change of the mode of polymorphic transition during crystn., which has been confirmed by in situ ATR-FTIR (ReactIR) spectroscopy in solution and in the solid state and by X-ray crystallog. anal. of their single crystals.

ED Entered STN: 16 Mar 2006
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1181576 CAPLUS
TITLE: Crystallization in final stages of purification
AUTHOR(S): Florence, Alastair J.; Shankland, Norman; Johnston, Andrea
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow, UK
SOURCE: Methods in Biotechnology (2005), 20(Natural Products Isolation (2nd Edition)), 275-295
CODEN: MEBIFQ
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Methods are described for the laboratory-scale crystn. of "small" organic compds. The process of crystn. from solution can be used as a purification step in its own right, or to produce crystals for mol. structure determination by single-crystal or powder X-ray diffraction. Both aspects are discussed, with particular emphasis on growing crystals for structure determination in natural product chemical. The processes detailed for the slow growth of diffraction-quality crystals include solvent selection and solution supersatn. by evaporation, cooling, liquid/vapor diffusion, and thermal gradient methods. Common problems and solns., including solid-state polymorphism and solvate formation, are highlighted and modern approaches to parallel crystn. and crystal structure determination from X-ray powder diffraction data are also introduced.

CC 9 (Biochemical Methods)
ST crystn purifn org compd
IT INDEXING IN PROGRESS
IT Impurities
Purification
Separation
(crystallization from solution as purification step)
IT Crystal structure
Crystal structure determination methods
Crystallization
X-ray diffraction
(crystallization from solution to produce crystals for mol. structure determination by single-crystal or powder X-ray diffraction)
IT Natural products
(crystallization from solution to produce crystals for mol. structure determination in

natural product chemical)
IT Crystal growth
(crystallization from solution to produce crystals for mol. structure determination with
particular emphasis on growing crystals)
AB Methods are described for the laboratory-scale crystn. of "small" organic compds. The process of crystn. from solution can be used as a purification step in its own right, or to produce crystals for mol. structure determination by single-crystal or powder X-ray diffraction. Both aspects are discussed, with particular emphasis on growing crystals for structure determination in natural product chemical The processes detailed for the slow growth of diffraction-quality crystals include solvent selection and solution supersatn. by evaporation, cooling, liquid/vapor diffusion, and thermal gradient methods. Common problems and solns., including solid-state polymorphism and solvate formation, are highlighted and modern approaches to parallel crystn. and crystal structure determination from X-ray powder diffraction data are also introduced.
ED Entered STN: 07 Nov 2005
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 43 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:953414 CAPLUS
DOCUMENT NUMBER: 143:311634
TITLE: Molecular interactions between solvent and pharmaceutical compounds in crystallization of polymorphic systems
AUTHOR(S): Mirmehrabi, Mahmoud; Rohani, Sohrab
CORPORATE SOURCE: Chemical and Biochemical Engineering Department, The University of Western Ontario, London, ON, N6A 5B9, Can.
SOURCE: AIChE Annual Meeting, Conference Proceedings, Austin, TX, United States, Nov. 7-12, 2004 (2004), 230B/1-230B/4. American Institute of Chemical Engineers: New York, N. Y.
CODEN: 69GSKT; ISBN: 0-8169-0965-2
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
AB Polymorphism in pharmaceutical solids is a major issue that has medical, financial and legal implications. There are many thermodn. and kinetics factors which affect the polymorph selectivity during the crystallization process such as nucleation temperature, supersatn. and type of solvent. Among these parameters, type of solvent is a major kinetic factor that has drawn the attention of researchers. Literature is ripe with research showing the effect of solvent on the polymorph selectivity, mainly using the polar and non-polar terminol., but seldom the researchers have explained the effect of solvent at mol. level. This work looks into the effect of solvent and the corresponding intermol. interactions on the polymorphic selectivity. Two case studies on the effect of solvent will be discussed for polymorphic systems of stearic acid (used for tablet coating) and ranitidine hydrochloride (H2-receptor antagonist drug).
CC 63-5 (Pharmaceuticals)
ST stearic acid ranitidine hydrochloride polymorphism crystn solvent effect
IT Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
(mol. interactions between solvent and pharmaceutical compds. in crystn. of polymorphic systems)
IT 57-11-4, Stearic acid, biological studies 66357-59-3, Ranitidine hydrochloride
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mol. interactions between solvent and pharmaceutical compds. in crystallization of polymorphic systems)
IT Crystallization
Hydrogen bond
Polymorphism (crystal)
Solvent effect
(mol. interactions between solvent and pharmaceutical compds. in crystn. of polymorphic systems)
ED Entered STN: 01 Sep 2005
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 66 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:123501 CAPLUS
DOCUMENT NUMBER: 143:352899
TITLE: Effect of crystal form on bioavailability
AUTHOR(S): Sohn, Young Taek
CORPORATE SOURCE: College of Pharmacy, DukSung Women's University, Seoul, 132-714, S. Korea
SOURCE: Yakche Hakhoechi (2004), 34(6), 443-452
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Korean
AB A review. Habit is the description of the outer appearance of a crystal. If the environment of a growing crystal affects its external shape without changing its internal structure, a different habit results. Crystal habit and the internal structure of a drug can affect bulk and physicochem. properties, which range from flowability to chemical stability. A polymorph is a solid cryst. phase of a given compound resulting from the possibility of at least two different arrangements of the mols. of that compound in the solid state. Chemical stability and solubility changes due to polymorphism can have an impact on a drug's bioavailability and its development program. During crystn. from a solution, crystals separating may consist of a pure component or be a mol. compound Solvates are mol. complexes that have incorporated the crystallizing solvent mol. in their lattice. When the solvent incorporated in the solvate is water, it is called a hydrate. To distinguish solvates from polymorphs, which are not mol. compds., the term pseudopolymorph is used. Identification of possible hydrate compds. is important since their aqueous solubilities can be significantly less than their anhydrous forms. Conversion of an anhydrous compound to a hydrate within the dosage form may reduce the dissoln. rate and extent of drug absorption. An amorphous solid may be treated as a supercooled liquid in which the arrangement of mols. is random. Amorphous solids lack the three-dimensional long-range order found in cryst . solids. Since amorphous forms are usually of higher thermodn. energy than corresponding cryst. forms, solubilities as well as dissoln. rates are generally greater. A study on crystal form includes characterization of (1)crystal habit, (2) polymorphism, (3)pseudopolymorphism, (4)amorphous solid.
CC 63-0 (Pharmaceuticals)
ST review drug crystal polymorphism bioavailability
IT Crystallization
Dissolution
Drug bioavailability
Polymorphism (crystal)
(effects of drug crystal forms on bioavailability)
IT Polymorphism (crystal)
(pseudopolymorphism; effects of drug crystal forms on bioavailability)
AB A review. Habit is the description of the outer appearance of a

crystal. If the environment of a growing crystal affects its external shape without changing its internal structure, a different habit results. Crystal habit and the internal structure of a drug can affect bulk and physicochem. properties, which range from flowability to chemical stability. A polymorph is a solid cryst. phase of a given compound resulting from the possibility of at least two different arrangements of the mols. of that compound in the solid state. Chemical stability and solubility changes due to polymorphism can have an impact on a drug's bioavailability and its development program. During crystn. from a solution, crystals separating may consist of a pure component or be a mol. compound Solvates are mol. complexes that have incorporated the crystallizing solvent mol. in their lattice. When the solvent incorporated in the solvate is water, it is called a hydrate. To distinguish solvates from polymorphs, which are not mol. compds., the term pseudopolymorph is used. Identification of possible hydrate compds. is important since their aqueous solubilities can be significantly less than their anhydrous forms. Conversion of an anhydrous compound to a hydrate within the dosage form may reduce the dissoln. rate and extent of drug absorption. An amorphous solid may be treated as a supercooled liquid in which the arrangement of mols. is random. Amorphous solids lack the three-dimensional long-range order found in cryst . solids. Since amorphous forms are usually of higher thermodn. energy than corresponding cryst. forms, solubilities as well as dissoln. rates are generally greater. A study on crystal form includes characterization of (1)crystal habit, (2) polymorphism, (3)pseudopolymorphism, (4)amorphous solid.

ED Entered STN: 14 Feb 2005

L18 ANSWER 73 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1015991 CAPLUS
DOCUMENT NUMBER: 142:11554
TITLE: Neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin
INVENTOR(S): Chandiran, Thakashina Moorty; Shobana, Jothi; Senthil, Kumar Minor
PATENT ASSIGNEE(S): Shasun Chemicals and Drugs Limited, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004101489	A1	20041125	WO 2003-IN246	20030721

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2003259544	A1	20041203	AU 2003-259544	20030721
EP 1636163	A1	20060322	EP 2003-816962	20030721

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: IN 2003-MA416 A 20030519
WO 2003-IN246 W 20030721

AB The present invention relates to the process for the preparation of anhydrous Gabapentin of pharmaceutical grade from the Gabapentin acid addition salts. The process consists of neutralizing the said acid addition salts with an organic base in water to get an aqueous solution comprising of Gabapentin and amine acid addition salt dissolved in water. The process further comprises of a method to sep. the Gabapentin and the amine acid addition salt from such an aqueous solution and to recover Gabapentin as an anhydrous Gabapentin form II.

IC ICM C07C061-06
ICS C07C061-08
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 24, 75
ST gabapentin neutralization crystn prepn crystal polymorphism
IT Amines, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(bases; in a neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT Distillation
Filtration
Precipitation (chemical)
(in a neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT Crystallization
Neutralization
Polymorphism (crystal)
Recrystallization
(neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT Bases, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(organic; in a neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT Alcohols, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvents; in a neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)
IT Amines, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(tertiary, bases; in a neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT 102-69-2, Tripropylamine 102-82-9, Tributylamine 121-44-8, Triethylamine, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT 60142-96-3P, Gabapentin
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT 60142-95-2, Gabapentin hydrochloride 797762-15-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(neutralization and crystallization process for the preparation of a polymorphic crystal form of gabapentin)
IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 71-36-3, Butyl alcohol, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)

(solvent; in a neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)

IT Alcohols, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvents; in a neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 71-36-3, Butyl alcohol, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvent; in a neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; neutralization and crystn. process for the preparation of a polymorphic crystal form of gabapentin)

ED Entered STN: 25 Nov 2004

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 78 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:766279 CAPLUS
DOCUMENT NUMBER: 141:384067
TITLE: Role of crystallization in the manufacturing of active pharmaceutical ingredients and in pharmaceutical technology
AUTHOR(S): Farkas, Bela; Szabo-Revesz, Piroska; Horvath, Karoly; Toreki-Zakanyi, Ildiko; Nagy, Kalman; Gregor, Tamas
CORPORATE SOURCE: EGIS Gyogyszergyar Rt., Hung.
SOURCE: Magyar Kemikusok Lapja (2004), 59(8), 264-270
CODEN: MGKLAL; ISSN: 0025-0163
PUBLISHER: Magyar Kemikusok Egyesulet
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Hungarian

AB A review. This paper deals with the basic principles of industrial crystn. focusing on practical aspects. The relation between the point of views of manufacturing of active pharmaceutical ingredients and crystn., the effect of conditions of crystn. on the particle size distribution, polymorphism, the formation of amorphous structure, and the residual solvent content was studied. We demonstrate the advantages of spherical crystn. process as a relatively new technique. The spherical crystn. process can be used to produce the cryst. active drugs suitable for direct tablet-making or capsule-filling.

CC 63-0 (Pharmaceuticals)
ST review crystn drug manufg
IT Amorphous structure
Crystallization
Drugs
Particle size distribution
Polymorphism (crystal)
Precipitation (chemical)
Solubility
(crystallization in manufacturing of active pharmaceutical ingredients and in pharmaceutical technol.)

IT Crystallization
(thermal; crystallization in manufacturing of active pharmaceutical ingredients and in pharmaceutical technol.)

AB A review. This paper deals with the basic principles of industrial crystn. focusing on practical aspects. The relation between the point of views of manufacturing of active pharmaceutical ingredients and crystn., the effect of conditions of crystn. on the particle size distribution, polymorphism, the formation of amorphous structure, and the residual solvent content was studied. We demonstrate the advantages of spherical crystn. process as a relatively new technique. The spherical crystn. process can be used to produce the cryst. active drugs suitable for direct tablet-making or capsule-filling.

ED Entered STN: 21 Sep 2004

L18 ANSWER 90 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:461199 CAPLUS
DOCUMENT NUMBER: 141:337338
TITLE: Particle generation for pharmaceutical applications using supercritical fluid technology
AUTHOR(S): Fages, Jacques; Lochard, Hubert; Letourneau, Jean-Jacques; Sauceau, Martial; Rodier, Elisabeth
CORPORATE SOURCE: Chemical Engineering Laboratory for Particulate Solids, Ecole des Mines d'Albi-Carmaux, UMR-CNRS 2392, Albi, 81013, Fr.
SOURCE: Powder Technology (2004), 141(3), 219-226
CODEN: POTEBX; ISSN: 0032-5910
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. In the pharmaceutical industry, an even greater number of products are in the form of particulate solids. Their formation, formulation and the control of their user properties are still not well understood and mastered. Since the mid-1980s, a new method of powder generation has appeared involving crystn. with supercrit. fluids. Carbon dioxide is the most widely used solvent and its innocuity and "green" characteristics make it the best candidate for the pharmaceutical industry. Rapid Expansion of Supercrit. Solns. (RESS), Supercrit. Anti Solvent (SAS) and Particles from Gas Saturated Solns. (PGSS) are three families of processes which lead to the production of fine and monodisperse powders, including the possibility of controlling crystal polymorphism. For the RESS process, the sudden decompression of the fluid in which a solute has been dissolved is the driving force of nucleation. CO_2 is, however, a rather feeble solvent and this is obviously the main limitation of the development of RESS. In the SAS process, CO_2 acts as a non-solvent for inducing the crystn. of a solute from an organic solution The versatility of SAS (there is always a proper solvent-antisolvent couple for the studied solute) ensures future developments for very different types of materials. PGSS uses the fact that it is much easier to dissolve CO_2 in organic solns. (or melted compds.) than the contrary. It presents very promising perspectives of industrial development. After almost 20 yr of active research, and more than 10 yr of process development, this technol. is reaching maturity, and very soon com. drug produced by these techniques are likely to appear.

CC 63-0 (Pharmaceuticals)
ST review particle inhalant supercrit fluid
IT Supercritical fluids
(particle generation for pharmaceutical applications using supercrit. fluid technol.)

IT Drug delivery systems

(particles; particle generation for pharmaceutical applications using supercrit. fluid technol.)

AB A review. In the pharmaceutical industry, an even greater number of products are in the form of particulate solids. Their formation, formulation and the control of their user properties are still not well understood and mastered. Since the mid-1980s, a new method of powder generation has appeared involving crystn. with supercrit. fluids. Carbon dioxide is the most widely used solvent and its innocuity and "green" characteristics make it the best candidate for the pharmaceutical industry. Rapid Expansion of Supercrit. Solns. (RESS), Supercrit. Anti Solvent (SAS) and Particles from Gas Saturated Solns. (PGSS) are three families of processes which lead to the production of fine and monodisperse powders, including the possibility of controlling crystal polymorphism. For the RESS process, the sudden decompression of the fluid in which a solute has been dissolved is the driving force of nucleation. CO_2 is, however, a rather feeble solvent and this is obviously the main limitation of the development of RESS. In the SAS process, CO_2 acts as a non-solvent for inducing the crystn. of a solute from an organic solution The versatility of SAS (there is always a proper solvent-antisolvent couple for the studied solute) ensures future developments for very different types of materials. PGSS uses the fact that it is much easier to dissolve CO_2 in organic solns. (or melted compds.) than the contrary. It presents very promising perspectives of industrial development. After almost 20 yr of active research,. . .

ED Entered STN: 08 Jun 2004

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 108 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:140258 CAPLUS
TITLE: Polymorphism in "Ionic liquids"
AUTHOR(S): Rogers, Robin Don; Holbrey, John D.; Reichert, W. Matthew
CORPORATE SOURCE: Chemistry, University of Alabama, Tuscaloosa, AL, USA
SOURCE: Abstracts, 38th Midwest Regional Meeting of the American Chemical Society, Columbia, MO, United States, November 5-7 (2003), 364. American Chemical Society: Washington, D. C.
CODEN: 69ETUW
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Polymorphs of crystd. ionic liqs. (ILs - defined as salts which melt below 100 °C), give direct evidence for inhibition of crystn. in these 'neoteric' solvents. The presence of two cryst. polymorphs of a common IL suggests crystal-packing frustration may be at least one reason for the tendency for ILs to remain as super-cooled liqs. which generally crystallize in a sluggish manner. In addition, since the two polymorphs have distinct, and non-mixing crystal lattices, then the formation of a eutectic liquid region below the m.ps. of both polymorphs might be anticipated from competition between the two cryst. forms. This presentation will introduce ionic liqs. and the information available to learn how the weak supramol. structures relate to liquid solvent behavior.

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ED Entered STN: 20 Feb 2004

L18 ANSWER 118 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:726613 CAPLUS
DOCUMENT NUMBER: 139:369499
TITLE: High-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compounds.
AUTHOR(S): Almarsson, Oern; Hickey, Magali B.; Peterson, Matthew L.; Morissette, Sherry L.; Soukasene, Stephen; McNulty, Chris; Tawa, Mark; MacPhee, J. Michael; Remenar, Julius F.
CORPORATE SOURCE: TransForm Pharmaceuticals, Inc., Lexington, MA, 02421, USA
SOURCE: Crystal Growth & Design (2003), 3(6), 927-933
CODEN: CGDEFU; ISSN: 1528-7483
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Surveys of crystal form diversity of two test compds., 1 (an exptl. angiotensin II antagonist) and 2 (sertraline HCl, the active drug in Zoloft), have been performed with high-throughput (HT) crystn. Compound 1 was found to have at least 18 crystal forms based on a HT recrystn. experiment using diverse solvents, compared with nine forms originally reported from a traditional screening effort. The efficiency of screening in HT mode is estimated to be about 2 orders of magnitude greater than traditional bench-scale approaches. The multiple patented forms of 2 have been summarized and evaluated based on published information, which is found to include several transient species and at least one mixture of known phases. A comparison between results of HT expts. and data on the disclosed forms shows that the HT effort generates the viable crystal forms; highly unstable hydrates and one metastable polymorph IV were not observed In attempting to recover form IV, a novel acetic acid solvate was discovered and characterized by single crystal X-ray diffraction. Addnl., a previously undisclosed Et acetate hemisolvate of 2 was identified as an intermediate en route to form T1. The study demonstrates that highly polymorphic pharmaceutical compds. can be surveyed by HT form experimentation, and that an HT strategy coupled with critical anal. of reported form diversity can be used to rank the utility of crystal forms.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 75
ST high throughput crystn polymorphism pharmaceutical
IT High throughput screening
(crystallization; high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)
IT Crystal morphology
(high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)
IT Polymorphism (crystal)
(in pharmaceutical compds.; high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)
IT Drugs
(polymorphic; high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)
IT 620168-87-8 620168-89-0
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)

IT 79559-97-0, Sertraline hydrochloride 186755-29-3
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphism; high-throughput surveys of crystal form diversity of highly polymorphic pharmaceutical compds.)

AB Surveys of crystal form diversity of two test compds., 1 (an exptl. angiotensin II antagonist) and 2 (sertraline HCl, the active drug in Zoloft), have been performed with high-throughput (HT) crystn . Compound 1 was found to have at least 18 crystal forms based on a HT recrystn. experiment using diverse solvents, compared with nine forms originally reported from a traditional screening effort. The efficiency of screening in HT mode is estimated to be about 2 orders of magnitude greater than traditional bench-scale approaches. The multiple patented forms of 2 have been summarized and evaluated based on published information, which is found to include several transient species and at least one mixture of known phases. A comparison between results of HT expts. and data on the disclosed forms shows that the HT effort generates the viable crystal forms; highly unstable hydrates and one metastable polymorph IV were not observed In attempting to recover form IV, a novel acetic acid solvate was discovered and characterized by single crystal X-ray diffraction. Addnl., a previously undisclosed Et acetate hemisolvate of 2 was identified as an intermediate en route to form T1. The study demonstrates that highly polymorphic pharmaceutical compds. can be surveyed by HT form experimentation, and that an HT strategy coupled with critical anal. of reported form diversity can be used to rank the utility of crystal forms.

ED Entered STN: 17 Sep 2003
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 124 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:641415 CAPLUS
DOCUMENT NUMBER: 139:372065
TITLE: A computer simulation based screening method for crystallization processes
AUTHOR(S): Thome, V.; Herrmann, M.; Pontius, H.; Kempa, P. B.; Doerich, M.
CORPORATE SOURCE: Fraunhofer Institut fuer Chemische Technologie, Pfinztal, D-76327, Germany
SOURCE: International Annual Conference of ICT (2003), 34th, 103/1-103/8
CODEN: IACIEQ; ISSN: 0722-4087
PUBLISHER: Fraunhofer-Institut fuer Chemische Technologie
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crystn. of organic solids from solns. is often a difficult task because phase transitions, formation of solvates or complexation could occur. Therefore it is important to find out solvent properties which have a pos. influence on the crystn. of desired polymorphs. As it is material and time consuming to determine solvent properties by exptl. methods we used a SGI Octane workstation equipped with the program Cerius 4.2 (Accelrys) for calculating solvent by force field (cff 91 950-1.01) and semiempirical methods (WinMopac). Moreover, a screening plan for the crystn. of nitramines was developed on the basis of 40 solvents, representing twelve different functional groups and the four influence factors: dipole moment, nonbond energy, molar volume and solvent polarity. It's known that the electrostatic potential of a mol. surface is related to solvent properties like the H-bond donating parameter α and the H-bond acceptor parameter β. It seems therefore necessary to include the electrostatic potential as an important influence factor. Crystn. expts. were carried out with .vepsiln.-CL-20 in a automated crystn. device Quest from Argonaut. The recrystd. samples were analyzed by x-ray diffraction (XRD), SEM, and DSC to characterize occurring polymorphs, donor-acceptor complexes and morphologies of the crystals. We found high correlations between polymorphic phases and solvent properties. Furthermore models and concepts for solution mechanism, complexation or decompns. of CL-20 were developed. The results and systematic evaluation allowed us to predict further suitable solvents for the crystn. of .vepsiln.-CL-20.

CC 75-1 (Crystallography and Liquid Crystals)
Section cross-reference(s): 50

ST CL 20 explosive crystn computer simulation screening

IT Crystallization
Simulation and Modeling
Solvent effect
(computer simulation based screening method for crystallization processes)

IT Explosives
(computer simulation based screening method for crystallization processes applied to .vepsiln.-CL-20)

IT 135285-90-4, CL-20
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(computer simulation based screening method for crystallization processes applied to .vepsiln.-CL-20)

AB Crystn. of organic solids from solns. is often a difficult task because phase transitions, formation of solvates or complexation could occur. Therefore it is important to find out solvent properties which have a pos. influence on the crystn. of desired polymorphs. As it is material and time consuming to determine solvent properties by exptl. methods we used a SGI Octane workstation equipped with the program Cerius 4.2 (Accelrys) for calculating solvent by force field (cff 91 950-1.01) and semiempirical methods (WinMopac). Moreover, a screening plan for the crystn. of nitramines was developed on the basis of 40 solvents, representing twelve different functional groups and the four influence factors: dipole moment, nonbond energy, molar volume and solvent polarity. It's known that the electrostatic potential of a mol. surface is related to solvent properties like the H-bond donating parameter α and the H-bond acceptor parameter β. It seems therefore necessary to include the electrostatic potential as an important influence factor. Crystn. expts. were carried out with .vepsiln.-CL-20 in a automated crystn. device Quest from Argonaut. The recrystd. samples were analyzed by x-ray diffraction (XRD), SEM, and DSC to characterize occurring polymorphs, donor-acceptor complexes and morphologies of the crystals. We found high correlations between polymorphic phases and solvent properties. Furthermore models and concepts for solution mechanism, complexation or decompns. of CL-20 were developed. The results and systematic evaluation allowed us to predict further suitable solvents for the crystn. of .vepsiln.-CL-20.

ED Entered STN: 18 Aug 2003
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 134 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:564320 CAPLUS
DOCUMENT NUMBER: 140:133465
TITLE: Crystallization of molecules. Consequences in terms of polymorphism and application in pharmaceutics. Basic concepts
AUTHOR(S): Bauer, M.
CORPORATE SOURCE: Departement international d'analyse, Sanofi Synthelabo Recherche, Toulouse, 31036, Fr.

SOURCE: S.T.P. Pharma Pratiques (2003), 13(2), 47-61
CODEN: SPPRER; ISSN: 1157-1497
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review. In this article, a brief description of the crystn. process is provided as well as definitions regarding polymorphism , pseudo-polymorphism and cryst. habit. After having recalled some basic aspects of physics and thermodn. of polymorphism and pseudo-polymorphism, the article discusses several examples: the strategy of cryst. form selection of a new chemical entity currently studied in clin. trials; the impact of the agglomeration/aggregation states of furosemide on the dissoln. of the corresponding tablets; the example of the taltireline crystn. taken from literature and investigating the impact of different parameters (in particular residual solvents) on the crystn. control. A brief introduction to the amorphous phases and their potential applications in the pharmaceutical domain is tackled as well as some regulatory considerations.

CC 63-0 (Pharmaceuticals)
ST review crystn polymorphism pharmaceutical
IT Crystallization
Drugs
Polymorphism (crystal)
(crystallization of mols. consequences in terms of polymorphism and application
in pharmaceutics)

AB A review. In this article, a brief description of the crystn. process is provided as well as definitions regarding polymorphism , pseudo-polymorphism and cryst. habit. After having recalled some basic aspects of physics and thermodn. of polymorphism and pseudo-polymorphism, the article discusses several examples: the strategy of cryst. form selection of a new chemical entity currently studied in clin. trials; the impact of the agglomeration/aggregation states of furosemide on the dissoln. of the corresponding tablets; the example of the taltireline crystn. taken from literature and investigating the impact of different parameters (in particular residual solvents) on the crystn. control. A brief introduction to the amorphous phases and their potential applications in the pharmaceutical domain is tackled as well as some regulatory considerations.

ED Entered STN: 24 Jul 2003
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 148 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:107138 CAPLUS
DOCUMENT NUMBER: 138:262829
TITLE: Toward Stereochemical Control, Monitoring, and Understanding of Crystal Nucleation
AUTHOR(S): Weissbuch, Isabelle; Lahav, Meir; Leiserowitz, Leslie
CORPORATE SOURCE: Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot, 76100, Israel
SOURCE: Crystal Growth & Design (2003), 3(2), 125-150
CODEN: CGDEFU; ISSN: 1528-7483
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB In this review, the delicate interplay between stereochem. control, monitoring at the subnanometer level, and an understanding of crystal nucleation is probed. Control of crystal nucleation may be achieved employing tailor-made auxiliaries, which are either nucleation inhibitors or promoters. The process may be monitored at an interface via grazing incidence x-ray diffraction (GIXD). By these means, the authors can glean exptl. knowledge of crystal nucleation in various mol. systems. A hypothesis was invoked that supersatd. solns. containing mol. clusters adopt various arrangements and shapes, some of which resemble the crystals into which they develop. This hypothesis was taken advantage of for the design of tailored inhibitors in achieving kinetic resolution of enantiomers and induced precipitation of particular crystal polymorphs. The control and behavior of polymorphic crystn. may be understood at the mol. level through the interplay between inhibitor, solvent, solute, and the surface layer crystal structures. With respect to promotion of crystal nucleation, it may be achieved by Langmuir monolayers at the air-aqueous solution interface, acting as a templating agent. Determination of the monolayer crystal structure by GIXD yields the extent and nature of the complementary fit between nucleator and nucleant. Finally, GIXD was applied to monitor by a snapshot technique the layer-by-layer cryst. assembly of cholesterol mols. at the air-H2O interface, which involved changes in mol. packing as the film grew in thickness.

CC 75-0 (Crystallography and Liquid Crystals)
ST review stereochem control monitoring understanding crystal nucleation
IT Crystallization
Polymorphism (crystal)
(control and behavior of polymorphic crystallization)
IT Langmuir monolayers
(in understanding of crystal nucleation)
IT Crystal nucleation
Stereochemistry
(toward stereochem. control, monitoring, and understanding of crystal nucleation)

AB In this review, the delicate interplay between stereochem. control, monitoring at the subnanometer level, and an understanding of crystal nucleation is probed. Control of crystal nucleation may be achieved employing tailor-made auxiliaries, which are either nucleation inhibitors or promoters. The process may be monitored at an interface via grazing incidence x-ray diffraction (GIXD). By these means, the authors can glean exptl. knowledge of crystal nucleation in various mol. systems. A hypothesis was invoked that supersatd. solns. containing mol. clusters adopt various arrangements and shapes, some of which resemble the crystals into which they develop. This hypothesis was taken advantage of for the design of tailored inhibitors in achieving kinetic resolution of enantiomers and induced precipitation of particular crystal polymorphs. The control and behavior of polymorphic crystn. may be understood at the mol. level through the interplay between inhibitor, solvent, solute, and the surface layer crystal structures. With respect to promotion of crystal nucleation, it may be achieved by Langmuir monolayers at the air-aqueous solution interface, acting as a templating agent. Determination of the monolayer crystal structure by GIXD yields the extent and nature of the complementary fit between nucleator and nucleant. Finally, GIXD was applied to monitor by a snapshot technique the layer-by-layer cryst. assembly of cholesterol mols. at the air-H2O interface, which involved changes in mol. packing as the film grew in thickness.

ED Entered STN: 12 Feb 2003
REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 163 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:497615 CAPLUS
DOCUMENT NUMBER: 137:201624
TITLE: FT-IR study on the effect of solvents on polymorphic crystallization of organic compounds
AUTHOR(S): Yamanobe, Maiko; Takiyama, Hiroshi; Matsuoka, Masakuni

CORPORATE SOURCE: Department of Chemical Engineering, Tokyo University of Agriculture and Technology, Tokyo, 184-8588, Japan
SOURCE: Journal of Chemical Engineering of Japan (2002), 35(6), 569-573
CODEN: JCEJAQ; ISSN: 0021-9592
PUBLISHER: Society of Chemical Engineers, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB FT-IR measurements of solns. of organic compds., which have several polymorphs, were carried out to discuss the effects of solvents on polymorphic crystn. DL-Methionine (DL-Met) and bisphenol A (BPA) were used as model compds. For DL-Met, characteristic peaks of IR spectra of solns. after reaction crystn . with various acids agreed with those of obtained crystals. The difference of IR spectra between solns. indicates that mol. conformations of DL-Met have already changed in the solns. before crystn. and were affected by the acids used for the reaction crystns. In the case of BPA, IR spectra of solns. with various solvents were measured to examine the effects of solvents on polymorphic crystn. Solns. with benzene and ethylbenzene showed similar characteristic peaks each other and form II crystals precipitated from benzene solns. while amorphous solid was obtained from ethylbenzene solns. Form I crystd. from other solns. without characteristic peaks. From these results, FT-IR measurement of solns. was concluded to be a useful anal. method to examine the effect of solvents on selective crystn. of polymorphs.

CC 35-2 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 22, 73, 75
ST methionine bisphenol crystn solvent FT IR
IT Crystallization
Polymorphism (crystal)
(FT-IR study on polymorphic crystallization of organic compds.)
IT IR spectroscopy
(Fourier-transform; FT-IR study on polymorphic crystallization of organic compds.)
IT Acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(effect of acids on polymorphic crystallization of methionine)
IT Dipole moment
(of solvent on polymorphic crystallization of bisphenol A)
IT Solvent effect
(on polymorphic crystallization of bisphenol A)
IT 64-19-7, Acetic acid, reactions 65-85-0, Benzoic acid, reactions 7647-01-0, Hydrochloric acid, reactions 41863-30-3, DL-Methionine sodium salt
RL: RCT (Reactant); RACT (Reactant or reagent)
(FT-IR study on effect of acids on polymorphic crystallization of organic compds.)
IT 59-51-8P, Methionine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(FT-IR study on polymorphic crystallization of organic compds.)
IT 80-05-7, Bisphenol A, processes
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(solvent effect on polymorphic crystallization of)

AB FT-IR measurements of solns. of organic compds., which have several polymorphs, were carried out to discuss the effects of solvents on polymorphic crystn. DL-Methionine (DL-Met) and bisphenol A (BPA) were used as model compds. For DL-Met, characteristic peaks of IR spectra of solns. after reaction crystn . with various acids agreed with those of obtained crystals. The difference of IR spectra between solns. indicates that mol. conformations of DL-Met have already changed in the solns. before crystn. and were affected by the acids used for the reaction crystns. In the case of BPA, IR spectra of solns. with various solvents were measured to examine the effects of solvents on polymorphic crystn. Solns. with benzene and ethylbenzene showed similar characteristic peaks each other and form II crystals precipitated from benzene solns. while amorphous solid was obtained from ethylbenzene solns. Form I crystd. from other solns. without characteristic peaks. From these results, FT-IR measurement of solns. was concluded to be a useful anal. method to examine the effect of solvents on selective crystn. of polymorphs.

ED Entered STN: 02 Jul 2002
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 164 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:493654 CAPLUS
DOCUMENT NUMBER: 138:276024
TITLE: New perspectives for the on-line monitoring of pharmaceutical crystallization processes using in situ infrared spectroscopy
AUTHOR(S): Fevotte, Gilles
CORPORATE SOURCE: Laboratoire Automatique et de Genie des Procedes, Universite Lyon, Villeurbanne, 69622, Fr.
SOURCE: International Journal of Pharmaceutics (2002), 241(2), 263-278
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion. Chemists and engineers involved in the industrial production of solid drugs have to deal with difficult new challenges, including the online mastery of the crystal habits and size distribution, the control of polymorphic transitions or the improvement of the chemical purity. A major limitation to improving the control of industrial crystallizers lies in the lack of versatile, accurate and reliable online sensors. It is shown that supersatn. measurements can be performed using in situ ATR mid-IR spectroscopy thus providing valuable real-time information about the crystn. process. Several case studies are presented to illustrate new potential applications of the technique. The reported exptl. results outline recent advances in the acquisition of key data characterizing the solute/solvent system in question (i.e. solubility, metastability, phase transformations...), the design of online control strategies capable of improving both the crystal size distribution and the reproducibility of the quality of the final product, the assessment of improved operating strategies (e.g. seeding batch crystallizers), and the monitoring of polymorphic transitions during cooling crystn. operations. The possibility of evaluating online the process impurities, which could allow the reduction of batch-to-batch variations of the quality of the solid product, is also briefly envisaged.

CC 63-0 (Pharmaceuticals)
ST review pharmaceutical online crystn IR spectroscopy
IT Crystallization
IR spectroscopy
(new perspectives for online monitoring of pharmaceutical crystallization processes using in situ IR spectroscopy)

AB A review and discussion. Chemists and engineers involved in the industrial production of solid drugs have to deal with difficult new challenges, including the online mastery of the crystal habits and size distribution, the control of polymorphic transitions or the improvement of the chemical purity. A major limitation to improving the

control of industrial crystallizers lies in the lack of versatile, accurate and reliable online sensors. It is shown that supersatn. measurements can be performed using in situ ATR mid-IR spectroscopy thus providing valuable real-time information about the crystn. process. Several case studies are presented to illustrate new potential applications of the technique. The reported exptl. results outline recent advances in the acquisition of key data characterizing the solute/ solvent system in question (i.e. solubility, metastability, phase transformations...), the design of online control strategies capable of improving both the crystal size distribution and the reproducibility of the quality of the final product, the assessment of improved operating strategies (e.g. seeding batch crystallizers), and the monitoring of polymorphic transitions during cooling crystn. operations. The possibility of evaluating online the process impurities, which could allow the reduction of batch-to-batch variations of the quality of the solid product, is also briefly envisaged.

ED Entered STN: 01 Jul 2002

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 172 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2002:189383 CAPLUS
TITLE:	Polymorph Selection: The role of additives and solvents
AUTHOR(S):	Blagden, Nicholas
CORPORATE SOURCE:	School of Pharmacy, University of Bradford, Bradford, UK
SOURCE:	Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), IEC-110. American Chemical Society: Washington, D. C. CODEN: 69CKQP
DOCUMENT TYPE:	Conference; Meeting Abstract
LANGUAGE:	English

AB Polymorph Selection: The role of additives and solvents
Nicholas Blagden, School of Pharmacy, U. of Bradford, Bradford, West Yorkshire BD7 1DP, UK, tel: +44(0)1274 234765, email: n.blagden@brad.ac.uk
Crystal engineering is currently a very topical area of research, with many dramatic examples of target architectures in the literature. For the vast number of cases reported the crystal engineering strategies used to generate the desired architecture must also generate a significant number of unplanned architectures. Even though the trend is to use a synthon with a stereo chemical which shows durability for a specific architecture. McCrone's statement that the number of polymorphs relates to the time spent looking for them covers the possibility of unplanned architectures being observed In crystal engineering terms this may be written as the time spent looking for a specific architecture the more likely that a variation in the behavior of the synthon will be observed For crystal engineering to achieve its goal of being able to select a specific mol. assembly based on synthon stereochem., the self-assembly of other viable assemblies would need to discouraged. The implication of this observation is that polymorph selection procedures must also be included into a crystal engineering strategy. The work in my talk will present some of the options available for predisposing a solution crystn. for one particular polymorph. For example, the issue maybe that two possibilities of assembly exist for the chosen synthon, YC(R)ZH, either chain or a dimer and the chain assembly is preferred over that of a dimer. How an understanding of polymorph selection may be used in crystal engineering for this type of situation will be examined

AB Polymorph Selection: The role of additives and solvents
Nicholas Blagden, School of Pharmacy, U. of Bradford, Bradford, West Yorkshire BD7 1DP, UK, tel: +44(0)1274 234765, email: n.blagden@brad.ac.uk
Crystal engineering is currently a very topical area of research, with many dramatic examples of target architectures in the literature. For the vast number of cases reported the crystal engineering strategies used to generate the desired architecture must also generate a significant number of unplanned architectures. Even though the trend is to use a synthon with a stereo chemical which shows durability for a specific architecture. McCrone's statement that the number of polymorphs relates to the time spent looking for them covers the possibility of unplanned architectures being observed In crystal engineering terms this may be written as the time spent looking for a specific architecture the more likely that a variation in the behavior of the synthon will be observed For crystal engineering to achieve its goal of being able to select a specific mol. assembly based on synthon stereochem., the self-assembly of other viable assemblies would need to discouraged. The implication of this observation is that polymorph selection procedures must also be included into a crystal engineering strategy. The work in my talk will present some of the options available for predisposing a solution crystn. for one particular polymorph. For example, the issue maybe that two possibilities of assembly exist for the chosen synthon, YC(R)ZH, either chain or a dimer and the chain assembly is preferred over that of a dimer. How an understanding of polymorph selection may be used in crystal engineering for this type of situation will be examined

ED Entered STN: 17 Mar 2002

L18 ANSWER 179 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2002:41527 CAPLUS
DOCUMENT NUMBER:	136:202341
TITLE:	Control of solvent-mediated transformation of crystal polymorphs using a newly developed batch crystallizer (WWDJ-crystallizer)
AUTHOR(S):	Shan, Gu; Igarashi, Koichi; Noda, Hideo; Ooshima, Hiroshi
CORPORATE SOURCE:	Department of Bioapplied Chemistry, Osaka City University, Sumiyoshi-ku, Osaka, 558-8585, Japan
SOURCE:	Chemical Engineering Journal (Amsterdam, Netherlands) (2002), 85(2-3), 169-176 CODEN: CMEJAJ; ISSN: 1385-8947
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Using a newly developed batch crystallizer (WWDJ-crystallizer) equipped with a slurry sprinkler named Wall Wetter and a double-deck jacket, a suppression of the solvent-mediated transformation of the metastable polymorphic crystals was attempted. Crystn. of l-glutamic acid was carried out to show an example of the suppression. The target polymorphic crystals, the metastable α-form crystals were exclusively obtained from the aqueous solution without transformation to the stable β-form polymorph even at a temperature where the transformation could not be avoided if a conventional batch crystallizer was used. The characteristic size of crystals obtained by WWDJ-crystallizer was large and their size distribution was narrow, comparing with those obtained by a conventional crystallizer.

CC 48-1 (Unit Operations and Processes)
Section cross-reference(s): 34, 45, 75

ST solvent transformation crystal polymorph batch crystallizer WWDJ

IT Crystallization
(batch; control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)

IT Crystallization apparatus
Crystallization temperature
Particle size distribution
Polymorphism (crystal)
(control of solvent-mediated transformation of

crystal polymorphs using newly developed batch
crystallizer)
IT 56-86-0P, L-Glutamic acid, processes
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)
(control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)
AB Using a newly developed batch crystallizer (WWDJ-crystallizer) equipped with a slurry sprinkler named Wall Wetter and a double-deck jacket, a suppression of the solvent-mediated transformation of the metastable polymorphic crystals was attempted.
Crystn. of l-glutamic acid was carried out to show an example of the suppression. The target polymorphic crystals, the metastable α-form crystals were exclusively obtained from the aqueous solution without transformation to the stable β-form polymorph even at a temperature where the transformation could not be avoided if a conventional batch crystallizer was used. The characteristic size of crystals obtained by WWDJ-crystallizer was large and their size distribution was narrow, comparing with those obtained by a conventional crystallizer.
IT Crystallization
(batch; control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)
IT Crystallization apparatus
Crystallization temperature
Particle size distribution
Polymorphism (crystal)
(control of solvent-mediated transformation of crystal polymorphs using newly developed batch crystallizer)
ED Entered STN: 16 Jan 2002
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 185 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:812707 CAPLUS
DOCUMENT NUMBER: 137:67958
TITLE: Modification of crystal habit and its role in dosage form performance
AUTHOR(S): Tiwary, A. K.
CORPORATE SOURCE: Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, India
SOURCE: Drug Development and Industrial Pharmacy (2001), 27(7), 699-709
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Crystn. is often employed for purifying a drug substance. Use of different solvents and processing conditions may change the crystal habit, besides altering the polymorphic state. Furthermore, altered habit may result from crystal growth during storage. Hence, there is a need to understand the factors influencing crystal habit and to evaluate critically its role in the performance of dosage forms. Establishing the physicotech. properties of different habits of a drug will help to recognize lot-to-lot variations in raw materials and to ensure reproducibility of dosage form performance.
CC 63-0 (Pharmaceuticals)
ST review crystal drug delivery system
IT Crystal morphology
Drug delivery systems
(modification of crystal habit and role in dosage form performance)

AB A review. Crystn. is often employed for purifying a drug substance. Use of different solvents and processing conditions may change the crystal habit, besides altering the polymorphic state. Furthermore, altered habit may result from crystal growth during storage. Hence, there is a need to understand the factors influencing crystal habit and to evaluate critically its role in the performance of dosage forms. Establishing the physicotech. properties of different habits of a drug will help to recognize lot-to-lot variations in raw materials and to ensure reproducibility of dosage form performance.
ED Entered STN: 08 Nov 2001
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 206 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:662268 CAPLUS
DOCUMENT NUMBER: 133:195206
TITLE: Crystallisation of Polymorphs: Thermodynamic Insight into the Role of Solvent
AUTHOR(S): Threlfall, Terry
CORPORATE SOURCE: Chemistry Department, University of York, Heslington York, YO10 5DD, UK
SOURCE: Organic Process Research & Development (2000), 4(5), 384-390
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dependent on the conditions, crystallization of polymorphs from solvent can be under kinetic or thermodn. control. In the latter case the nature of the solvent is immaterial in respect of the polymorph produced. The conditions under which each of these factors may apply are analyzed in detail. The transition point between two dimorphs may not present a sharp divide in which crystallization above and below the transition temperature
produces the
high melting and the low melting polymorph, resp. It is shown that even in those cases where the choice of solvent appears to be critical this may be a secondary effect related to the concentration attainable in that solvent at a certain temperature rather than a specific effect dependent on solvent-solute interaction. A corollary to these considerations is the necessity to determine solubility curves and metastable zone widths in order to be able to control polymorph crystallization
CC 48-1 (Unit Operations and Processes)
Section cross-reference(s): 69
ST crystn polymorph solvent thermodn
IT Crystallization
Polymorphism (crystal)
Solvents
Thermodynamics
(thermodn. insight into role of solvent in crystn. of polymorphs)
IT Crystallization
Polymorphism (crystal)
Solvents
Thermodynamics
(thermodn. insight into role of solvent in crystn. of polymorphs)
ED Entered STN: 22 Sep 2000
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 211 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:537889 CAPLUS
DOCUMENT NUMBER: 133:245192

TITLE: Crystallization and polymorphism of conformationally flexible molecules. Problems, patterns, and strategies
AUTHOR(S): Yu, Lian; Reutzel-Edens, Susan M.; Mitchell, Christine A.
CORPORATE SOURCE: Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Organic Process Research & Development (2000), 4(5), 396-402
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 59 refs. Two effects of conformational flexibility on crystn., namely conformational polymorphism and reduction of crystn. tendency, are discussed using examples from the literature and our own studies. The preferred mol. conformations observed in several polymorphic systems are correlated with the nature of the forces present in the crystals. The reduction of crystn. tendency for conformationally flexible mols. arises from the presence of multiple conformers in the crystallizing media and the need for certain mols.
to
crystallize in high-energy conformations. Despite their peculiarities, the control of crystn. of conformationally flexible mols. should begin with traditional approaches applicable to most crystn. situations. However, special techniques, including conformational mimicry, solvent-mediated self-assembly, and templated growth, were devised to introduce mol.-level control to the crystn. process.

CC 75-0 (Crystallography and Liquid Crystals)
ST review crystn polymorphism conformationally flexible mol
IT Conformation
Conformational transition
Crystallization
Molecular crystals
Polymorphism (crystal)
(crystallization and polymorphism of conformationally flexible mols.)

AB A review with 59 refs. Two effects of conformational flexibility on crystn., namely conformational polymorphism and reduction of crystn. tendency, are discussed using examples from the literature and our own studies. The preferred mol. conformations observed in several polymorphic systems are correlated with the nature of the forces present in the crystals. The reduction of crystn. tendency for conformationally flexible mols. arises from the presence of multiple conformers in the crystallizing media and the need for certain mols.
to
crystallize in high-energy conformations. Despite their peculiarities, the control of crystn. of conformationally flexible mols. should begin with traditional approaches applicable to most crystn. situations. However, special techniques, including conformational mimicry, solvent-mediated self-assembly, and templated growth, were devised to introduce mol.-level control to the crystn. process.

ED Entered STN: 07 Aug 2000
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 216 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:263770 CAPLUS
DOCUMENT NUMBER: 133:4293
TITLE: Polymorphism and pseudopolymorphism in organic crystals. A cambridge structural database study
AUTHOR(S): Sarma, Jagarlapudi A. R. P.; Desiraju, Gautam R.
CORPORATE SOURCE: Physical and Inorganic Chemistry Division, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SOURCE: NATO ASI Series, Series C: Mathematical and Physical Sciences (1999), 539(Crystal Engineering: The Design and Application of Functional Solids), 325-356
CODEN: NSCSDW; ISSN: 0258-2023
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with .apprx.25 refs. An anal. with the Cambridge Structural Database (CSD) of polymorphism among single residue organic and organometallic entries reveals that the likelihood of the phenomenon is low and more significantly, does not vary with the C content of the mol. in the range C1 to C80. Larger mols. with a larger number of potential recognition sites during crystn. also cascade into their stable crystal structures more efficiently than do smaller mols. In effect, polymorphism is fat less of a problem in crystal engineering and related disciplines than was held previously. Compds. that contain conformationally flexible groups which can also form strong H bonds, for example -OH and -NH2 are more likely to occur in polymorphic forms. A description of polymorphism in terms of patterns of similar or dissimilar supramol. synthons is also given. Polymorphism occurs when the same synthon can be constructed in different ways. This can happen when there are multiple occurrences of the same functional group in a mol. The phenomenon of pseudopolymorphism also was examined with the CSD. The inclusion of H2O in organic crystals is especially common while CH2Cl2 is included in organometallics. Other H bonding solvents like DMSO, DMF and dioxane are also included frequently. When the occurrence of pseudopolymorphism is corrected for solvent usage, it appears that EtOH and hexane occur in crystals far less than their usage as recrystn. solvents might indicate. Certain compds. like resorcinol, pyrazine-2-carboxamide and N-2-thiazolylsulfanilamide show strikingly different polymorphic forms. Yet, in the end, polymorphism is essentially a random phenomenon and only certain combinations of mol. size, shape and functionality, or in a supramol. sense, a particular flexibility in synthon construction can lead to its occurrence.

CC 22-0 (Physical Organic Chemistry)
Section cross-reference(s): 75
ST review polymorphism pseudopolymorphism org crystal cambridge database
IT Polymorphism (crystal)
(cambridge structural database study of polymorphism and pseudopolymorphism in organic crystals)
IT Crystals
(organic; cambridge structural database study of polymorphism and pseudopolymorphism in organic crystals)

AB A review, with .apprx.25 refs. An anal. with the Cambridge Structural Database (CSD) of polymorphism among single residue organic and organometallic entries reveals that the likelihood of the phenomenon is low and more significantly, does not vary with the C content of the mol. in the range C1 to C80. Larger mols. with a larger number of potential recognition sites during crystn. also cascade into their stable crystal structures more efficiently than do smaller mols. In effect, polymorphism is fat less of a problem in crystal engineering and related disciplines than was held previously. Compds. that contain conformationally flexible groups which can also form strong H bonds, for example -OH and -NH2 are more likely to occur in polymorphic forms. A description of polymorphism in terms of patterns of similar or dissimilar supramol. synthons is also given. Polymorphism occurs when the same synthon can be constructed in different ways. This can happen when there are multiple occurrences of the same functional group in a mol. The phenomenon of pseudopolymorphism also was examined with the CSD. The inclusion of H2O in organic crystals is especially common while CH2Cl2 is included in organometallics. Other H bonding solvents like DMSO DMF and dioxane are also included frequently. When the occurrence of pseudopolymorphism is corrected for solvent usage, it appears that

EtOH and hexane occur in crystals far less than their usage as recrystn. solvents might indicate. Certain compds. like resorcinol, pyrazine-2-carboxamide and N-2-thiazolylsulfanilamide show strikingly different polymorphic forms. Yet, in the end, polymorphism is essentially a random phenomenon and only certain combinations of mol. size, shape and functionality, or in a supramol. sense, a particular flexibility in synthon construction can lead to its occurrence.

ED Entered STN: 24 Apr 2000

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 245 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:479493 CAPLUS
DOCUMENT NUMBER: 129:81537
TITLE: Preparation of alternate crystal forms of gabapentin
INVENTOR(S): Pesachovich, Michael; Singer, Claude; Pilarski, Gideon
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9828255	A1	19980702	WO 1997-US23164	19971224

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 119890	A1	20020310	IL 1996-119890	19961224
CA 2275912	AA	19980702	CA 1997-2275912	19971224
AU 9857990	A1	19980717	AU 1998-57990	19971224
EP 950044	A1	19991020	EP 1997-954134	19971224

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6255526	B1	20010703	US 1999-331555	19990622
PRIORITY APPLN. INFO.:			IL 1996-119890 A	19961224
			WO 1997-US23164 W	19971224

AB Gabapentin hydrochloride, free of inorg. salts, is converted to a different crystal structure of gabapentin (referred to as crystal structure form II) by: (1) obtaining gabapentin hydrochloride that is free of inorg. salts; (2) mixing a solution of the gabapentin hydrochloride with an addnl. amine in a first solvent so as to obtain a precipitate comprising gabapentin; and (3) recovering the desired gabapentin form II from the polymorphic precipitate The precipitated gabapentin is a novel polymorphic form of gabapentin possessing a cryst. structure characterized by novel sets of peaks in its powder X-ray diffraction pattern and in the FTIR spectra. The recovery step may comprise one of two alternative methods, slurrying the initial gabapentin in methanol, and then filtering the suspension to obtain gabapentin form II, or solubilizing the gabapentin form III in methanol with heating by reflux, and then cooling the solution to obtain gabapentin form II by crystn.

IC ICM C07C061-06

CC 24-5 (Alicyclic Compounds)
Section cross-reference(s): 75

ST gabapentin crystal structure polymorphism; crystn gabapentin crystal structure polymorphism

IT Crystal structure
Polymorphism (crystal)
(preparation of alternate crystal forms of gabapentin)

IT Crystallization
(preparation of alternate crystal forms of gabapentin via)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alternate crystal forms of gabapentin via reaction with)

IT 60142-96-3P, Gabapentin
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation of alternate crystal forms of gabapentin)

IT 60142-95-2, Gabapentin hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alternate crystal forms of gabapentin)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 71-36-3, 1-Butanol, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 75-65-0, tert-Butanol, uses 78-93-3, Mek, uses 100-46-9, Benzylamine, uses 100-51-6, Benzyl alcohol, uses 102-69-2, Tripropylamine 102-82-9, Tributylamine 102-86-3, Trihexylamine 108-21-4, Isopropyl acetate 108-88-3, Toluene, uses 109-86-4, Ethylene glycol monomethyl ether 109-89-7, Diethylamine, uses 121-44-8, Triethylamine, uses 127-19-5, Dimethylacetamide 141-43-5, Ethanolamine, uses 141-78-6, Ethyl acetate, uses 616-38-6, Dimethyl carbonate 35296-72-1, Butanol
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of alternate crystal forms of gabapentin)

AB Gabapentin hydrochloride, free of inorg. salts, is converted to a different crystal structure of gabapentin (referred to as crystal structure form II) by: (1) obtaining gabapentin hydrochloride that is free of inorg. salts; (2) mixing a solution of the gabapentin hydrochloride with an addnl. amine in a first solvent so as to obtain a precipitate comprising gabapentin; and (3) recovering the desired gabapentin form II from the polymorphic precipitate The precipitated gabapentin is a novel polymorphic form of gabapentin possessing a cryst. structure characterized by novel sets of peaks in its powder X-ray diffraction pattern and in the FTIR spectra. The recovery step may comprise one of two alternative methods, slurrying the initial gabapentin in methanol, and then filtering the suspension to obtain gabapentin form II, or solubilizing the gabapentin form III in methanol with heating by reflux, and then cooling the solution to obtain gabapentin form II by crystn.

ED Entered STN: 03 Aug 1998

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 259 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:477003 CAPLUS
DOCUMENT NUMBER: 127:150362
TITLE: Crystal science techniques in the manufacture of chiral compounds
AUTHOR(S): Wood, W. M. L.
CORPORATE SOURCE: ZENECA Huddersfield Works, Huddersfield, UK
SOURCE: Chirality in Industry II (1997), 119-156. Editor(s): Collins, Andrew N.; Sheldrake, G. N.; Crosby, J. Wiley: Chichester, UK.
CODEN: 64TBAW
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review, with 29 refs., on application of crystn. principles to large-scale production of chiral compds. Crystal,

polymorphs and solvates, and crystal habits and modifiers; crystn. processes [supersatn., solvent choice, solubility curves, nucleation and crystal size control]; and isolation of metastable phases are discussed. Separation of enantiomers by diastereoisomer formation, separation of diastereoisomers, and resolution by direct crystn. of enantiomers, are also discussed.

CC 45-0 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
Section cross-reference(s): 75

ST review crystn process chiral compd manuf; supersatn soly crystn control review; enantiomer sepn crystn review

IT Crystal morphology
Crystallization
Diastereomers
Resolution (separation)
Supersaturation
(crystallization principles and processes in manufacture of chiral compds.)

AB A review, with 29 refs., on application of crystn. principles to large-scale production of chiral compds. Crystal, polymorphs and solvates, and crystal habits and modifiers; crystn. processes [supersatn., solvent choice, solubility curves, nucleation and crystal size control]; and isolation of metastable phases are discussed. Separation of enantiomers by diastereoisomer formation, separation of diastereoisomers, and resolution by direct crystn. of enantiomers, are also discussed.

ED Entered STN: 31 Jul 1997

L18 ANSWER 268 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:55240 CAPLUS
DOCUMENT NUMBER: 126:148257
TITLE: Crystallization behavior and functionalities of pharmaceutical and food materials
AUTHOR(S): Yamamoto, Hideji
CORPORATE SOURCE: Dep. Food Sci. & Technology, Faculty Engin., Fukuyama Univ., Fukuyama, 729-02, Japan
SOURCE: Nippon Kessho Seicho Gakkaishi (1996), 23(5), 422-429
CODEN: NKSGDK; ISSN: 0385-6275
PUBLISHER: Nippon Kessho Seicho Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 44 refs. This article reviews recent studies on the crystn. phenomena and operation for the preparation of pharmaceuticals and functional foods. Main interests are focused on selective crystn. of polymorphs and solvent mediated phase transition, clathrative crystn. of green tea polyphenol with cyclodextrin, crystn. of maltose accompanying anomerization process, crystallinity and functionalities of drug, and the modification of crystal habits by controlling agitation condition for improvement of separation by filtration.

CC 63-0 (Pharmaceuticals)

ST review crystn pharmaceutical food

IT Crystallization
Drug delivery systems
Food
(crystallization behavior and functionalities of pharmaceutical and food materials)

AB A review with 44 refs. This article reviews recent studies on the crystn. phenomena and operation for the preparation of pharmaceuticals and functional foods. Main interests are focused on selective crystn. of polymorphs and solvent mediated phase transition, clathrative crystn. of green tea polyphenol with cyclodextrin, crystn. of maltose accompanying anomerization process, crystallinity and functionalities of drug, and the modification of crystal habits by controlling agitation condition for improvement of separation by filtration.

ED Entered STN: 25 Jan 1997

L18 ANSWER 289 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:510762 CAPLUS
DOCUMENT NUMBER: 122:252333
TITLE: Understanding and control of nucleation, growth, habit, dissolution and structure of two- and three-dimensional crystals using 'tailor-made' auxiliaries
AUTHOR(S): Weissbuch, Isabelle; Popovitz-Biro, Ronit; Lahav, Meir; Leiserowitz, Leslie
CORPORATE SOURCE: Dep. Mater. Interfaces, Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Acta Crystallographica, Section B: Structural Science (1995), B51(2), 115-48
CODEN: ASBSDK; ISSN: 0108-7681
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with many refs. Tailor-made auxiliaries for the control of nucleation and growth of mol. crystals may be classified into two broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes, which include morphol. engineering and etching, reduction of crystal symmetry, assignment of absolute structure of chiral mols. and polar crystals, elucidation of the effect of solvent on crystal growth, and crystn. of a desired polymorph. As for crystal growth promoters, monolayers of amphiphilic mols. on H_2O were used to induce the growth of a variety of three-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or electrostatic interaction. A particular focus is made on the induced nucleation of ice by monolayers of H_2O-insol. aliphatic alcs. The two-dimensional cryst. structures of such monolayers were studied by grazing incidence x-ray diffraction. It has become possible to monitor, by this method, the growth, dissoln. and structure of self-aggregated cryst. monolayers, and indeed multilayers, affected by the interaction of solvent mols. in the aqueous subphase with the amphiphilic headgroups, and using tailor-made amphiphilic additives.

CC 75-0 (Crystallography and Liquid Crystals)

ST review nucleation growth morphol structure crystal; dissoln crystal review

IT Crystal growth
Crystal morphology
Crystal nucleation
Crystal structure
Solution process
(understanding and control of nucleation, growth, habit, dissoln. and structure of two- and three-dimensional crystals using tailor-made auxiliaries)

AB A review, with many refs. Tailor-made auxiliaries for the control of nucleation and growth of mol. crystals may be classified into two broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes, which include morphol. engineering and etching, reduction of crystal symmetry, assignment of absolute structure of chiral mols. and polar crystals, elucidation of the effect of solvent on crystal growth, and crystn. of a desired polymorph. As for crystal growth promoters, monolayers of amphiphilic mols. on H_2O were used to induce the growth of a variety of three-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or electrostatic interaction. A particular focus is made on the induced nucleation of ice by monolayers of H_2O-insol. aliphatic alcs. The two-dimensional cryst. structures of such monolayers were studied by grazing incidence x-ray diffraction.

It has become possible to monitor, by this method, the growth, dissoln. and structure of self-aggregated cryst. monolayers, and indeed multilayers, affected by the interaction of solvent mols. in the aqueous subphase with the amphiphilic headgroups, and using tailor-made amphiphilic additives.
ED Entered STN: 26 Apr 1995

L18 ANSWER 298 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:19392 CAPLUS
DOCUMENT NUMBER: 120:19392
TITLE: Tailor-made auxiliaries for the control of nucleation, growth and dissolution of two- and three-dimensional crystals
AUTHOR(S): Lahav, M.; Leiserowitz, L.
CORPORATE SOURCE: Dep. Mater. Interfaces, Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Journal of Physics D: Applied Physics (1993), 26(8B), B22-B31
CODEN: JPAPBE; ISSN: 0022-3727
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 51 refs. Tailor-made mol. auxiliaries for the control of nucleation and growth of mol. crystals may be classified into 2 broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes which include morphol. engineering, reduction of crystal symmetry, assignment of absolute structure of polar crystals, elucidation of the effect of solvent on crystal growth and crystn. of a desired polymorph. As for crystal growth promoters, Langmuir monolayers on water have been used to induce growth of 3-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or an electrostatic interaction. The 2-dimensional cryst. structures of these monolayers have been studied by grazing-incidence x-ray diffraction (GIXD). It has become possible to monitor, by GIXD, the growth and dissoln. of self-aggregated cryst. monolayers affected by the interaction of solvent mols. in the aqueous subphase with the monolayer headgroups.
CC 75-0 (Crystallography and Liquid Crystals)
ST review crystal nucleation growth dissoln inhibitor; promoter crystal nucleation growth dissoln review; nucleation crystal inhibitor promoter review; growth crystal inhibitor promoter review; dissoln crystal inhibitor promoter review
IT Crystal growth
Crystal nucleation
Crystallization
Solution process
(of two- and three-dimensional mol. crystals, tailor-made inhibitors and promoters for)
IT Solvent effect
(on crystal growth and crystn. of polymorphs)
AB A review with 51 refs. Tailor-made mol. auxiliaries for the control of nucleation and growth of mol. crystals may be classified into 2 broad categories: inhibitors and promoters. Tailor-made inhibitors of crystal growth can be used for a variety of purposes which include morphol. engineering, reduction of crystal symmetry, assignment of absolute structure of polar crystals, elucidation of the effect of solvent on crystal growth and crystn. of a desired polymorph. As for crystal growth promoters, Langmuir monolayers on water have been used to induce growth of 3-dimensional crystals at the monolayer-solution interface by structural match, mol. complementarity or an electrostatic interaction. The 2-dimensional cryst. structures of these monolayers have been studied by grazing-incidence x-ray diffraction (GIXD). It has become possible to monitor, by GIXD, the growth and dissoln. of self-aggregated cryst. monolayers affected by the interaction of solvent mols. in the aqueous subphase with the monolayer headgroups.
IT Solvent effect
(on crystal growth and crystn. of polymorphs)
ED Entered STN: 08 Jan 1994

L18 ANSWER 348 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:554023 CAPLUS
DOCUMENT NUMBER: 97:154023
TITLE: Solvent effects in crystallization processes
AUTHOR(S): Davey, R. J.
CORPORATE SOURCE: ICI Corp. Lab., Runcorn/Cheshire, UK
SOURCE: Current Topics in Materials Science (1982), 8, 429-79
CODEN: CTMSD2; ISSN: 0165-1854
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 59 refs., including nucleation, crystal size, crystal habit, and polymorphism.
CC 75-0 (Crystallography and Liquid Crystals)
Section cross-reference(s): 48
ST review crystn solvent effect; nucleation crystal solvent effect review; morphol crystal solvent effect crystn review; polymorphism solvent effect crystn review
IT Solvent effect
(in crystallization process)
IT Crystal nucleation
Crystallization
(solvent effects in)
IT Crystal form
Polymorphism
(solvent effects in crystallization in relation to)
ST review crystn solvent effect; nucleation crystal solvent effect review; morphol crystal solvent effect crystn review; polymorphism solvent effect crystn review
ED Entered STN: 12 May 1984

L18 ANSWER 377 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:414899 CAPLUS
DOCUMENT NUMBER: 67:14899
TITLE: Application of infrared absorption spectroscopy for the examination of drugs and their preparations. XVII. Polymorphism of J. P. pharmaceuticals. 3
AUTHOR(S): Oba, Takuma; Koyama, Ryoko
SOURCE: Eisei Shikensho Hokoku (1966), No. 84, 4-7
CODEN: ESKHA5; ISSN: 0077-4715
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB cf. preceding abstract Four cryst. forms of barbital and 2 cryst. forms of phenobarbital were obtained when they were recrystd. from various solvents. Their polymorphism was reflected by the ir absorption patterns from 650 to 3600 cm.-1. The formation of solvation complexes is suggested.
CC 64 (Pharmaceutical Analysis)
ST IR DRUGS POLYMORPHISM; POLYMORPHISM DRUGS IR; DRUGS POLYMORPHISM IR; SOLVATION COMPLEXES DRUGS; COMPLEXES SOLVATION DRUGS; BARBITAL SOLVATION COMPLEXES; PHENOBARBITAL SOLVATION COMPLEXES
IT 50-06-6, properties 57-44-3
RL: PRP (Properties)
(spectroscopy (ir) of, polymorphism and)
AB cf. preceding abstract Four cryst. forms of barbital and 2

cryst. forms of phenobarbital were obtained when they were recrystd. from various solvents. Their polymorphism was reflected by the ir absorption patterns from 650 to 3600 cm.-1. The formation of solvation complexes is suggested.

ED Entered STN: 12 May 1984

L18 ANSWER 378 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1967:79541 CAPLUS
DOCUMENT NUMBER: 66:79541
TITLE: Data on the development of the optimal crystal shape of basic pharmaceutical materials
AUTHOR(S): Nikolics, Karoly; Bidlo, Gabor; Nikolics, Mrs. Karoly
CORPORATE SOURCE: Tech. Univ. Budapest, Budapest, Hung.
SOURCE: Acta Pharmaceutica Hungarica (1967), 37(1), 20-4
CODEN: APHGAO; ISSN: 0001-6659
DOCUMENT TYPE: Journal
LANGUAGE: Hungarian

AB The influence of solvents and solvent mixts. on crystal shape of some pharmaceutical products was studied. Derivs. of salicylic, carbamic, and barbituric acids were crystd . from hot supersatd. solution The crystals were studied by x-ray, and in some cases by ir spectrography. The micro m.ps. of the polymorph compds. were determined The use of seed crystals and the order of solvents used in the crystn. process play a role in the development of structure.

CC 63 (Pharmaceuticals)

ST CRYSTAL SHAPES DRUGS; DRUGS CRYSTAL SHAPES

IT Solvents, properties
(crystallization of barbituric, carbamic and salicylic acid derivs. in)

IT 60-29-7, properties
RL: PRP (Properties)
(crystallization of barbituric carbamic and salicylic acid derivs. in)

IT 64-17-5, properties 67-56-1, properties 67-66-3, properties
RL: PRP (Properties)
(crystallization of barbituric, carbamic and salicylic acid derivs. in)

IT 67-52-7D, Barbituric acid, derivs. 69-72-7, Salicylic acid 463-77-4, Carbamic acid
RL: BIOL (Biological study)
(solvent effect on crystals of)

AB The influence of solvents and solvent mixts. on crystal shape of some pharmaceutical products was studied. Derivs. of salicylic, carbamic, and barbituric acids were crystd . from hot supersatd. solution The crystals were studied by x-ray, and in some cases by ir spectrography. The micro m.ps. of the polymorph compds. were determined The use of seed crystals and the order of solvents used in the crystn. process play a role in the development of structure.

ED Entered STN: 12 May 1984

L18 ANSWER 433 OF 464 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1954:46259 CAPLUS
DOCUMENT NUMBER: 48:46259
ORIGINAL REFERENCE NO.: 48:8230a-h
TITLE: Infrared spectra of organic compounds exhibiting polymorphism
AUTHOR(S): Ebert, A. A., Jr.; Gottlieb, H. B.
CORPORATE SOURCE: E. I. du Pont de Nemours & Co., Wilmington, DE
SOURCE: Journal of the American Chemical Society (1952), 74, 2806-10
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The α- (I) and β-forms (II) of phthalocyanine and their Cu (III and IV), Ni (V and VI), Zn (VII and VIII), and Co (IX and X) salts were prepared Thus 82 g. phthalonitrile (XI) and 10.6 g. Cu bronze were heated at 137-40° for 24 hrs. in 400 ml. (CH2OH)2, cooled to 80° and drowned in EtOH, the solids filtered off and extracted with EtOH. The EtOH was displaced with H2O and the aqueous press-cake slurried with H2O containing concentrated NH4OH and 0.5 g. NH4Cl for 1.5 hrs. at 70° to give a 77% yield of III. III is unstable in aromatic solvents. XI (155 g.), 315 ml. PhNO2, 49.6 g. anhydrous CuSO4, and 13 g. (NH4)2SO4 were heated to 105° and a stream of NH3 passed through, the mixture heated to 225-30° over 0.5 hr. and held there for 5 hrs. to give crude IV, which was isolated by filtration and washing with MeOH. Milling of crude IV with NaCl and Tetralin gave IV as a finely divided pigment. o-C6H4(CO)2O (120 g.), 180 g. CO(NH2)2, 49.7 g. NiCl2.6H2O, 0.5 g. (NH4)2Mo7O24, and 200 ml. C6H3Cl3 were heated at 200° for 4.5 hrs. and the residue extracted with 1% HCl for 1.5 hrs. at 70° to give crude VI, which was similarly milled to a fine powder and extracted with Me2CO in a Soxhlet to give V which in turn was milled with dry NaCl. XI (128 g.), 18 g. Zn powder, and 450 ml. C6H3Cl3 were heated to 200° during 1 hr. and kept there for 12 hrs. to give after working up VII and VIII. VII was easily transformed into VIII by heating for 8 hrs. in refluxing Me2CO. IX and X were synthesized by reacting Co metal with XI in (CH2OH)2 at 190°. I and II were synthesized by known methods (cf. U.S. 2,485,167, C.A. 44, 10336i; U.S. 2,556,729, C.A. 45, 9269b). Three organic compds. were also obtained in crystn. modifications: 2,4-Cl(O2N)C6H3CO2H when crystd. from C6H6 gave modification A (XII); a slowly cooled melt of the acid produced modification B (XIII). The 2 forms (XIV and XV) of allylthiourea were similarly obtained. Crystn. of anthranilic acid gave modification A (XVI). The commercial acid consisted chiefly of modification B (XVII) whereas modification C (XVIII) was obtained from the melt. The x-ray diffraction patterns of I-X and XII-XVIII were determined in order to characterize the polymorphic crystal modifications whose infrared spectra were measured. The distinctive patterns show that the crystals of all the investigated modifications were well developed, excepting those of IX and X. The infrared spectra of I-X in a Nujol suspension were given; there was marked similarity between the α- and β-modifications in the 3-8 micron range with noticeable differences among the skeletal frequencies, especially at 12.5-14.5 microns. The transformation of III into IV in cyclohexanol was followed at room temperature by the change in infrared absorption. The time required for complete conversion was 90 min. The spectra for the crystal modifications of XII-XVIII were scanned in a Nujol suspension. Marked differences were apparent between the spectra of the different modifications. However when XII-XVIII were in solution the spectra were found to be identical for all the modifications of the compound in solution Therefore infrared spectrometry is a useful tool for studying polymorphism.

CC 10 (Organic Chemistry)

IT Polymorphism
(of organic compds., spectra and)

IT Spectra
(polymorphism and, of organic compds.)

IT 574-93-6, Phthalocyanine
(and derivs., polymorphism and spectra of)

IT 7440-48-4, Cobalt
(compds., with phthalocyanines, polymorphism and spectra of)

IT 99-60-5, Benzoic acid, 2-chloro-4-nitro- 109-57-9, Thiosinamine 118-92-3, Anthranilic acid 7440-02-0, Nickel, compound with α-phthalocyanine 7440-02-0, Nickel, compound with β-phthalocyanine 7440-66-6, Zinc, compound with α-phthalocyanine 7440-66-6, Zinc, compound with β-phthalocyanine
(polymorphism and spectra of)

AB . . . 80° and drowned in EtOH, the solids filtered off and extracted with EtOH. The EtOH was displaced with H2O and the aqueous press-cake slurried with H2O containing concentrated NH4OH and 0.5 g. NH4Cl for 1.5 hrs. at

70° to give a 77% yield of III. III is unstable in aromatic solvents. XI (155 g.), 315 ml. $PhNO_2$, 49.6 g. anhydrous $CuSO_4$, and 13 g. $(NH_4)_2SO_4$ were heated to 105° and a stream of NH_3 passed through, the mixture heated to 225-30° over 0.5 hr. and held there for 5 hrs. to give crude IV, which was isolated by filtration and washing. . . VIII by heating for 8 hrs. in refluxing Me_2CO. IX and X were synthesized by reacting Co metal with XI in $(CH_2OH)_2$ at 190°. I and II were synthesized by known methods (cf. U.S. 2,485,167, C.A. 44, 10336i; U.S. 2,556,729, C.A. 45, 8269b). Three organic compds. were also obtained in crystn. modifications: 2,4-$Cl(O_2N)C_6H_3CO_2H$ when crystd. from C_6H_6 gave modification A (XII); a slowly cooled melt of the acid produced modification B (XIII). The 2 forms (XIV and XV) of allylthiourea were similarly obtained. Crystn. of anthranilic acid gave modification A (XVI). The commercial acid consisted chiefly of modification B (XVII) whereas modification C (XVIII) was obtained from the melt. The x-ray diffraction patterns of I-X and XII-XVIII were determined in order to characterize the polymorphic crystal modifications whose infrared spectra were measured. The distinctive patterns show that the crystals of all the investigated modifications were well developed, excepting those of IX and X. The infrared spectra of I-X in a Nujol suspension were given; there was marked similarity between the α- and β-modifications in the 3-8 micron range with noticeable differences among the skeletal frequencies, especially at 12.5-14.5 microns. The transformation of III into IV in cyclohexanol was followed at room temperature by the change in infrared absorption. The time required for complete conversion was 90 min. The spectra for the crystal modifications of XII-XVIII were scanned in a Nujol suspension. Marked differences were apparent between the spectra of the different modifications. However when XII-XVIII were in solution the spectra were found to be identical for all the modifications of the compound in solution Therefore infrared spectrometry is a useful tool for studying polymorphism.

ED Entered STN: 22 Apr 2001